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DETERMINATION OF THE BASAL METABOLISM FROM THE CARBON-DIOXIDE ELIMINATION

By John T. King, Jr.

WITH A STATISTICAL NOTE

By Raymond Pearl

(From the Medical Clinic of The Johns Hopkins Hospital)

Estimation of the basal metabolism is evolving rapidly into a common laboratory and even bedside procedure. Since it was found by Lusk, Benedict, DuBois and others, that measurement of the oxygen and carbon-dioxide gas exchange offers a method for calculating the heat production that compares favorably with direct observation in the chamber calorimeter, many gas exchange methods have been developed. At least three of these are based upon the measurement of both oxygen intake and carbon-dioxide elimination. The "Tissot" method described fully by Boothby and Sandiford,[1] is an "open" method, the patient inhaling fresh air through a valve and the exhaled air being subjected to gas analysis for remaining oxygen and eliminated carbon-dioxide. The "universal respiration apparatus" has been evolved under Benedict[2] into a "portable" apparatus, a "closed" system which affords a method for direct measurement of oxygen consumption by volume and also for the measurement of carbon-dioxide elimination by weight. A combined chamber and respiration apparatus is in use at New Haven.[3] It has been customary, when both oxygen and carbon-dioxide figures are obtained, to calculate the heat production in calories from the oxygen consumption, taking into consideration the respiratory quotient.

More recent methods deal with the oxygen consumption only, a respiratory quotient of 0.82 being assumed. Apparatuses for the measurement of oxygen alone have been proposed by Benedict and Collins[4] and by Jones,[5] and simplified forms of apparatus for bedside use are being manufactured by commercial houses on their own initiative.

Although criticism of any method may, to a certain extent, be justifiable, some helpful information can undoubtedly be obtained through the use of any one of them by a careful observer. The attempt is being widely made to find the most accurate, stable and simple method which at the same time is

[1] Boothby and Sandiford: Laboratory Manual of the Technic of Basal Metabolic Rate Determination. Saunders, Philadelphia, 1920.

[2] Benedict, F. G.: A Portable Respiration Apparatus for Clinical Use. Boston Med. and Surg. Jour., 1918, CCXXVIII, 667.

[3] Barbour, H. G.: Antipyretics. I. The Benedict Respiration Chamber at the New Haven Hospital. Arch. Int. Med., 1919, XXIV, 611.

[4] Benedict and Collins: A Clinical Apparatus for Measuring Basal Metabolism. Boston Med. & Surg. Jour., 1920, CLXXXIII, 449.

[5] Jones, H. M. A Simple Device for Measuring Basal Metabolism. Jour. Am. Med. Assn., 1920, LXXV, 538.

hygienic and relatively inexpensive for use in routine clinical examinations.

So far, it has not been suggested to make use of a simple measurement of the carbon-dioxide elimination as an index to the metabolic rate. Barbour,[5] however, who uses a combined box and Benedict respiration apparatus, states that he has found the carbon-dioxide elimination to be less variable than the oxygen consumption and has therefore been accustomed to calculate heat production from carbon-dioxide elimination. It seemed to us to be worth while to find out how valuable would be an index to the metabolic rate obtained by measuring carbon-dioxide elimination alone.

In order to determine this point, it seemed the best procedure to study the original chamber calorimetric work. By so doing, we are able to compare oxygen consumption with carbon-dioxide elimination and also to compare each of these factors with the heat production, as measured directly.

For this purpose 27 experiments have been analysed, 10 being taken from the publication of Benedict and Carpenter[6] and 17 from work by Sonderstrom, Meyer and DuBois.[7]

[6] Table I.
[7] Table II.

Each experiment represents an hour's observation, though in some repeated tests were made upon the same subject. Only observations upon resting subjects in the post-absorptive state were selected. In the case of the Benedict and Carpenter observations, the more recent DuBois height-weight formula for computing body surfaces was applied to data furnished in the published protocols.

The ten protocols of Benedict and Carpenter were analysed by the writer in Table I as follows: The average carbon-dioxide elimination per square meter per hour was determined (Col. A); the average oxygen consumption was determined (Col. B); and the average heat production was determined (Col.C). On the basis of these averages, the deviation of carbon-dioxide from its average was calculated for each experiment. The deviations of oxygen consumption and of heat production from their respective averages were also calculated for each experiment. The carbon-dioxide deviation from its average was then compared directly with the deviation of heat production from its average in each experiment. It was found that the average difference between carbon-dioxide variations and calorie variations was 4.93 per

TABLE I

DATA FROM BENEDICT AND CARPENTER

METABOLISM AND ENERGY TRANSFORMATION OF HEALTHY MEN

Pub. Carnegie Inst., 1910

Name	Height in cm.	Weight in kgm.	Body surface (height-wt. form)	Direct calorimetry						Deviation of CO_2 from average (in gms.)	Deviation of O_2 from average (in gms.)	Deviation of cals. from average (in cals.)
				A		B		C				
				CO_2 per hr. (gms.)	CO_2 per sq. m. per hr. (gms.)	O_2 per hr. in gms.	O_2 per sq. m. per hr. (gms.)	Cals. per hr.	Cals. per sq. m. per hr.			
C. R. Y.	170	67.8	1.78	29.35	16.45	25.9	14.55	97.2	54.6	+2.39	+2.36	+9.8
A. H. M.	179	65.3	1.83	24.80	13.56	20.5	11.20	81.3	44.5	—0.50	—0.99	—0.3
A. L. L.	166	67.5	1.75	23.50	13.42	17.8	10.17	81.0	46.3	—0.64	—2.02	+1.5
H. R. D.	171	58.2	1.69	25.65	15.20	25.6	15.15	74.65	44.2	+1.14	+2.96	—0.6
H. R. D.	171	58.2	1.69	22.55	13.32	17.3	10.23	67.9	40.2	—0.74	—1.96	—4.6
H. C. K.	181	73.0	1.93	25.95	13.45	23.6	12.23	87.65	45.4	—0.61	+0.04	+0.6
H. C. K.	181	73.0	1.93	25.45	13.20	22.1	11.45	82.25	42.6	—0.86	—0.74	—2.2
H. C. K.	181	73.0	1.93	28.70	14.87	25.0	12.95	83.35	43.2	+0.81	+0.76	—1.6
H. C. K.	181	73.0	1.93	26.40	13.68	22.3	11.55	85.85	44.5	—0.38	—0.64	—0.3
H. C. K.	181	73.0	1.93	26.10	13.62	24.1	12.48	83.4	43.2	—0.54	+0.29	—1.6
Total					140.67		121.96		448.7			
Average					14.06		12.19		44.8			

Name	Per cent variations of CO_2, O_2, and calories (direct method) computed from above data									Comparison of CO_2 variations with calorie variations and of O_2 variations with calorie variations		
	Deviation of CO_2 from average		Deviation of O_2 from average		Deviation of cals. from average						Deviation of CO_2 from cals. (per cent)	Deviation of O_2 from cals. (in per cent)
C. R. Y.	+17.0	.....	+19.3	.....	+21.9	.....	.....	.....	.....	.....	—4.90	— 2.6
A. H. M.	— 3.56	.....	— 8.1	.....	— 0.7	.....	.....	.....	.....	.....	—3.49	— 7.4
A. L. L.	— 4.51	.....	—16.5	.....	+ 3.3	.....	.....	.....	.....	.....	—7.81	—19.8
H. R. D.	+ 8.1	.....	+24.3	.....	— 1.4	.....	.....	.....	.....	.....	+9.50	+25.7
H. R. D.	— 5.26	.....	—16.1	.....	—10.3	.....	.....	.....	.....	.....	+5.04	— 5.8
H. C. K.	— 4.37	.....	+ 0.3	.....	+ 1.4	.....	.....	.....	.....	.....	—5.77	— 1.1
H. C. K.	— 6.12	.....	— 6.1	.....	— 4.9	.....	.....	.....	.....	.....	—1.22	— 1.2
H. C. K.	+ 5.76	.....	+ 6.2	.....	— 3.6	.....	.....	.....	.....	.....	+9.36	+ 9.8
H. C. K.	— 2.72	.....	— 5.2	.....	— 0.7	.....	.....	.....	.....	.....	—2.02	— 4.5
H. C. K.	— 3.84	.....	+ 2.4	.....	— 3.6	.....	.....	.....	.....	.....	—0.24	+ 6.0
										Total....	49.35	83.9
										Average.	4.93	8.39

TABLE II

DATA FROM SONDERSTROM, MEYER AND DUBOIS

Arch. Int. Med., 1916, V. 17, part 2, p. 872

Name	Indirect calorimetry												
	Body surface (Dubois linear formula)	A			B				C			Deviation of CO_2 from cals. in per ct.	Deviation of O_2 from cals. in per ct.
		CO_2 eliminated per hour (gms.)	CO_2 per sq. meter per hour (gms.)	Deviation of CO_2 from average (gms.)	Deviation of CO_2 from average (in per ct.)	O_2 used per hour per sq. m. (Gms.)	Deviation of O_2 from average (Gms.)	Deviation of O_2 from average (in per ct.)	Cals. per sq. m. per hour	Deviation of cals. from average	Deviation of cals. from average (in per ct.)		
A. G.	1.67	24.32	14.55	+1.34	+10.01	12.38	+0.45	+ 3.78	41.50	+3.03	+ 8.14	+1.87	— 4.36
A. G.	1.67	25.97	15.50	+2.29	+17.30	12.54	+0.61	+ 5.12	42.55	+4.08	+10.61	+6.69	— 5.49
A. G.	1.67	24.31	14.50	+1.29	+ 9.76	12.71	+0.78	+ 6.50	42.30	+3.83	+ 9.95	—0.19	— 3.45
A. G.	1.67	22.43	13.45	+0.24	+ 1.82	11.90	—0.03	— 0.25	39.80	+1.33	+ 3.46	—1.64	— 3.71
A. G.	1.67	25.06	15.05	+1.84	+13.92	12.20	+0.27	+ 2.25	41.40	+2.93	+ 7.62	+6.30	— 5.37
A. G.	1.67	24.92	14.90	+1.69	+12.80	13.65	+1.72	+14.41	45.30	+6.83	+17.75	—4.95	— 3.34
R. H. S.	1.83	23.21	12.68	—0.53	— 4.01	11.94	+0.01	+ 0.08	36.50	—1.97	— 5.13	+1.12	+ 5.21
R. H. S.	1.83	23.79	12.98	—0.23	— 1.74	12.51	+0.58	+ 4.85	38.10	—0.37	— 0.96	—0.78	+ 5.81
E. F. D. B.	1.91	23.43	12.29	—0.92	— 6.96	12.79	+0.86	+ 7.22	37.00	—1.47	— 3.82	—3.14	+11.04
E. F. D. B.	1.91	23.69	12.40	—0.81	— 6.13	13.18	+1.25	+10.50	38.05	—0.42	— 1.09	—5.04	+11.59
Wm. A.	1.80	25.32	14.08	+0.87	+ 6.59	12.17	+0.24	+ 2.00	38.50	+0.03	+ 0.08	+6.51	+ 1.92
Cardiac Pt.	1.80	24.08	13.38	+0.17	+ 1.29	12.52	+0.59	+ 4.95	38.95	+0.48	+ 1.25	+0.04	+ 3.70
(Restless)	1.80	24.45	13.60	+0.39	+ 2.92	13.19	+1.26	+10.50	40.70	+2.23	+ 5.79	—2.87	+ 4.71

DATA FROM GEPHARDT AND DUBOIS

Arch. Int. Med., Vol. XVII, Part 2, p. 902

Emma W.	1.64	18.22	11.12	—2.09	—15.82	9.85	—2.08	—17.44	33.25	—5.22	—13.56	—2.26	—3.88
(Woman)	....	18.41	11.22	—1.99	—15.07	9.68	—2.25	—18.85	32.87	—5.60	—14.55	—0.52	—4.30
	....	18.55	11.30	—1.91	—14.46	9.61	—2.32	—19.41	33.03	—5.44	—14.14	—0.32	—5.27
	....	18.86	11.50	—1.71	—12.94	10.30	—1.63	—13.68	34.25	—4.22	—10.97	—1.97	—2.71
Total	.....	.....	224.50			203.12			654.05			46.21	85.86
Average	.....	.....	13.21			11.93			38.47			2.72	5.05

Name	Direct calorimetry of preceding observations					Comparison of CO_2, O_2 and indirect calorie figures with direct calories		
	Body surface (linear formula)	C		Deviation of cals. from average (in cals.)	Deviation of cals. from average (in per cent)	Deviation of CO_2 from direct cals. (in per cent)	Deviation of O_2 from direct cals. (in per cent)	Deviation of indirect cals. from direct cals. (in per cent)
		Cals. per hour	Cals. per sq. m. per hour					
A. G.	1.67	69.44	41.58	+3.52	+ 9.2	+ 0.81	— 5.42	— 1.06
A. G.	....	72.03	43.13	+5.07	+13.3	+ 4.00	— 8.18	— 2.69
A. G.	....	73.58	44.06	+6.00	+15.6	— 5.84	— 9.10	— 5.65
A. G.	....	65.19	39.04	+0.98	+ 2.6	— 0.78	— 2.85	+ 0.86
A. G.	....	70.68	42.32	+4.26	+11.2	+ 2.72	— 8.95	— 3.58
A. G.	....	73.59	44.06	+6.00	+15.6	— 2.80	— 1.19	+ 2.15
R. H. S.	1.83	72.65	39.70	+1.64	+ 4.3	— 8.31	— 4.22	— 9.43
R. H. S.	....	71.40	39.02	+0.96	+ 2.5	— 4.24	+ 2.35	— 3.46
E. F. D. R.	1.91	69.89	36.59	—1.47	— 3.8	— 3.16	+11.02	— 0.02
E. F. D. R.	....	75.52	39.54	+1.48	+ 3.9	—10.03	+ 6.60	— 4.99
Wm. A.	1.80	62.29	34.60	—3.46	— 9.1	—15.69	+11.10	+ 9.18
Wm. A.	....	69.48	38.60	+0.54	+ 1.4	— 0.11	+ 3.19	— 0.15
Wm. A.	....	70.55	39.19	+1.13	+ 2.9	+ 0.02	+ 7.60	+ 2.89
Emma W.	1.64	54.38	33.16	—4.90	—12.9	— 2.92	— 4.54	— 0.66
Emma W.	....	49.73	30.32	—7.74	—20.3	+ 5.23	+ 1.45	+ 5.75
Emma W.	....	46.26	28.21	—9.85	—25.9	+11.44	+ 6.19	+11.76
Emma W.	....	55.75	33.99	—4.07	—10.7	— 2.24	— 2.98	— 0.27
Total	.....	.....	647.11			80.44	96.93	64.55
Average	.....	.....	38.06			4.73	5.70	3.79

cent. The average difference between oxygen variations and calorie variations was 8.39 per cent.

An analysis was made in a corresponding manner of the data of Sonderstrom, Meyer and DuBois. In this series the calories calculated by the "indirect method" are also published. It must be remembered that the technique of these early observations with the chamber calorimeter included not only the O_2 consumption and the CO_2 elimination but urinary nitrogen determination as well.

By these means, the nitrogenous metabolism was estimated, and the O_2 and CO_2 figures were partitioned and calculated for protein and non-protein oxidation. The "indirect method" used in connection with the chamber calorimeter may, therefore, be taken as ideal.

The analysis is shown in Table II. It will be seen that the average difference between the indirect calorimetric figures and the direct calorimetric figures amounts to 3.79 per cent. The average difference between CO_2 and direct calorimetric figures is 4.73 per cent. The average differences between O_2 and direct calorimetric figures is 5.70 per cent.

A third series of protocols was studied (Table III), chiefly for the purpose of obtaining a scale of standard figures for the

TABLE III

FROM THE BASAL, GASEOUS METABOLISM OF NORMAL MEN AND WOMEN

BENEDICT, EMMES, ROTH AND SMITH

Jour. Biol. Chem., Vol. XVIII, No. 2, July, 1914

NORMAL MEN

Name	Age	Weight in kgm.	Height in cm.	Body surface (DuBois)	A				B'			C'	
					CO_2 per min. (cc.)	CO_2 per hour (cc.)	CO_2 per hour (gms.)	CO_2 per sq. m. per hour (Gms.)	O_2 per min. (cc.)	O_2 per hr. (cc.)	O_2 per hr. per sq. m. (cc.)	Cals. total (24 hrs.)	Cals. per sq. m. (24 hrs.)
H. W.	19	108.9	198	2.43	326	19,560	38.43	15.82	361	21,660	8,914	2,559	1,053
W. S.	22	88.5	165	1.96	241	14,460	28.00	14.29	289	17,340	8,840	2,017	1,029
O. F. M.	24	85.8	121	1.98	209	12,540	24.62	12.46	265	15,900	8,030	1,827	922
F. G. B.	41	83.1	183	2.05	217	13,020	25.58	12.47	258	15,480	7,551	1,802	879
Prof. C.	36	83.0	169	1.93	199	11,940	23.43	12.17	237	14,220	7,370	1,655	857
J. H. R.	23	82.2	187	2.07	243	14,580	28.62	13.84	282	16,920	8,174	1,978	956
D. H. W.	22	82.1	186	2.06	245	14,700	28.93	14.03	291	17,460	8,473	2,034	987
H. F.	63	82.1	166	1.9	180	10,800	21.42	11.19	236	14,160	7,449	1,615	851
M. H. K.	19	79.0	188	2.05	243	14,580	28.62	13.98	276	16,560	8,075	1,944	949
E. G.	20	78.9	184	2.02	262	15,720	30.46	15.09	302	18,120	8,970	2,126	1,053
W. A. M.	23	78.0	183	2.0	213	12,780	25.03	12.52	262	15,720	7,860	1,816	907
Dr. M.	28	75.9	180	1.95	214	12,840	25.22	12.95	273	16,380	8,400	1,877	962
M. Ba.	20	75.0	180	1.94	221	13,260	26.20	13.52	263	15,780	8,130	1,837	947
F. E. M.	38	75.0	164	1.82	209	12,540	24.62	13.53	242	14,520	7,980	1,698	932
J. F. M.	20	74.5	181	1.95	227	13,620	26.78	13.73	269	16,140	8,280	1,878	963
F. A. R.	32	74.4	163	1.8	205	12,300	24.17	13.43	244	14,640	8,135	1,704	948
W. J. T.	22	74.2	183	1.95	206	12,360	24.23	12.43	256	15,360	7,875	1,770	908
F. G. R.	20	74.0	179	1.93	242	14,520	28.64	14.87	267	16,020	8,300	1,914	992
C. D. R.	22	74.0	173	1.88	238	14,280	28.02	14.92	270	16,200	8,620	1,908	1,015
H. R. W.	24	73.9	175	1.89	222	13,320	26.19	13.85	264	15,840	8,380	1,842	974
J. P. C.	23	73.7	169	1.85	186	11,160	21.90	11.85	218	13,080	7,070	1,526	825
A. O. G.	25	73.2	179	1.92	194	11,640	22.86	11.92	271	16,260	8,470	1,835	956
H. W. E.	23	73.0	168	1.83	190	11,400	22.39	12.23	222	13,320	7,275	1,559	852
P. D. F.	23	71.2	176	1.87	219	13,140	25.82	13.83	259	15,540	8,320	1,810	968
C. B. S.	26	71.1	179	1.89	202	12,120	23.83	12.63	244	14,640	7,740	1,700	899
J. H. H.	25	69.1	171	1.81	197	11,820	23.22	12.84	234	14,040	7,752	1,634	903
N. K. W.	35	68.4	166	1.77	196	11,760	23.08	13.06	219	13,140	7,425	1,549	875
B. A. W.	26	67.9	174	1.82	229	13,740	27.00	14.84	280	16,800	9,231	1,945	1,069
K. H. A.	26	66.4	182	1.86	199	11,640	22.87	12.32	238	14,280	7,675	1,654	889
J. R.	27	66.0	182	1.85	201	12,060	23.68	12.82	241	14,460	7,815	1,679	907
M. A. M.	29	66.0	177	1.81	206	12,360	24.26	13.42	242	14,520	8,025	1,695	937
F. P. R.	22	65.1	173	1.78	182	10,920	21.47	12.08	222	13,320	7,480	1,543	867
J. J. C.	27	65.0	175	1.79	190	11,400	22.38	12.49	227	13,620	7,610	1,585	886
E. H. T.	25	64.7	170	1.75	173	10,380	20.38	11.64	217	13,020	7,440	1,499	857
D. M.	22	64.0	171	1.75	187	11,220	22.05	12.62	240	14,400	8,225	1,651	944
M. J. S.	24	63.7	170	1.74	195	11,700	22.98	13.22	237	14,220	8,170	1,647	947
M. Y. B.	20	63.5	172	1.75	207	12,420	24.42	13.97	238	14,280	8,160	1,677	958
R. O. S.	21	63.5	170	1.74	205	12,300	24.17	13.88	228	13,680	7,860	1,619	930
E. P. C.	35	63.2	185	1.85	171	10,260	20.13	10.88	216	12,960	7,001	1,489	805
R. G.	23	62.7	173	1.75	194	11,640	22.87	13.08	227	13,620	7,780	1,590	908
U. R. B.	27	62.6	173	1.75	179	10,740	21.10	12.07	220	13,200	7,540	1,525	872
W. F. M.	21	62.4	180	1.80	221	13,260	26.03	14.48	259	15,540	8,640	1,816	1,009
H. H. A.	22	62.3	164	1.68	179	10,740	21.10	12.57	213	12,780	7,610	1,487	886
H. C. B.	27	62.0	173	1.74	192	11,520	22.63	13.03	239	14,340	8,240	1,653	950
S. A. R.	23	60.8	165	1.67	175	10,500	20.62	12.35	209	12,540	7,509	1,460	873
A. L.	40	60.6	171	1.71	191	11,460	22.52	13.17	225	13,500	7,890	1,576	922
W. G. J.	21	60.5	175	1.74	210	12,600	24.75	14.23	250	15,000	8,621	1,746	1,003
H. L. H.	26	60.5	172	1.72	200	12,000	23.58	13.71	244	14,640	8,511	1,696	985
J. E. F.	21	60.4	172	1.72	202	12,120	23.82	13.87	229	13,740	7,990	1,616	940
J. K. M.	24	60.4	173	1.73	182	10,920	21.44	12.42	223	13,380	7,730	1,549	895
H. B. R.	25	60.2	168	1.68	173	10,380	20.39	12.13	214	12,840	7,640	1,487	885
J. B. T.	20	60.1	171	1.71	209	12,540	24.63	14.42	251	15,060	8,810	1,748	1,022
W. F. B.	32	60.1	168	1.68	199	11,940	23.46	13.97	233	13,980	8,320	1,632	972
L. H. W.	27	60.0	179	1.76	184	11,040	21.70	12.34	219	13,140	7,470	1,530	869
H. B. L.	20	60.0	173	1.72	190	11,400	22.39	13.02	229	13,740	7,990	1,596	927
L. E. E.	31	59.8	175	1.73	204	12,240	24.06	13.93	245	14,700	8,490	1,707	987
F. M. M.	16	59.7	173	1.72	203	12,180	23.92	13.91	251	15,060	8,751	1,739	1,011
W. B. L.	29	59.3	164	1.65	165	9,900	19.43	11.77	211	12,660	7,670	1,451	879
T. H. Y.	22	59.2	169	1.68	190	11,400	22.39	13.32	231	13,860	8,250	1,605	955
D. R. S.	43	58.5	181	1.76	153	9,180	18.03	10.25	193	11,580	6,580	1,331	756
B. H.	39	58.2	178	1.73	166	9,960	19.56	11.32	200	12,000	6,930	1,393	806
D. J. M.	20	58.0	175	1.71	189	11,340	22.28	13.04	233	13,980	8,175	1,615	944
H. F. T.	32	57.8	179	1.73	165	9,900	19.43	11.24	192	11,520	6,660	1,348	779
E. T. W.	22	57.8	169	1.67	171	10,260	20.13	12.04	213	12,780	7,650	1,472	881
P. F. J.	20	57.2	167	1.64	193	11,580	22.74	13.87	232	13,920	8,480	1,616	985
L. D. A.	19	57.1	171	1.67	188	11,280	22.18	13.27	220	13,200	7,900	1,539	921
A. G. E.	26	57.0	169	1.65	195	11,700	22.99	13.93	216	12,960	7,850	1,531	928
R. I. C.	26	56.8	184	1.75	194	11,640	22.86	13.10	244	14,640	8,370	1,687	964
C. J. O.	27	56.7	160	1.58	...	.....	.....	.....	218	13,080	8,275	1,524	965

TABLE III—CONTINUED

Name	Age	Weight in kgm.	Height in cm.	Body surface (DuBois)	A				B′			C′	
					CO_2 per min. (cc.)	CO_2 per hour (cc.)	CO_2 per hour (gms)	CO_2 per sq. m. per hour (gms.)	O_2 per min. (cc.)	O_2 per hr. (cc.)	O_2 per hr. per sq. m. (cc.)	Cals. total (24 hrs.)	Cals. per sq. m. (24 hrs.)
J. W. P.	30	56.5	172	1.67	203	12,180	23.92	14.33	243	14,580	8,730	1,697	1,017
W. W. C.	17	56.3	172	1.66	199	11,940	23.46	14.17	232	13,920	8,386	1,629	980
W. A. S.	21	56.3	169	1.64	190	11,400	22.39	13.65	223	13,380	8,160	1,562	952
J. C. C.	22	56.1	173	1.67	179	10,740	21.10	12.64	219	13,140	7,870	1,522	912
Q. P. R.	41	52.2	164	1.56	158	9,480	18.63	11.93	193	11,580	7,420	1,341	859
O. N. A.	25	55.4	171	1.63	177	10,620	20.87	12.83	224	13,440	8,249	1,545	948
C. H. H.	19	55.1	169	1.63	173	10,380	20.39	12.52	203	12,180	7,475	1,421	872
I. A. F.	24	54.9	156	1.53	190	11,400	22.39	14.63	232	13,920	9,090	1,612	1,053
V. G.	17	54.3	162	1.57	198	11,880	23.34	14.86	233	13,980	8,900	1,632	1,040
A. F. G.	24	53.9	175	1.65	178	10,680	20.98	12.72	207	12,420	7,525	1,453	881
M. B.	27	53.6	160	1.54	170	10,200	20.03	13.02	210	12,600	8,182	1,455	945
L. E. A.	30	52.2	174	1.62	191	11,460	22.52	13.89	219	13,140	8,115	1,541	952
B. M. K.	27	51.4	163	1.54	164	9,840	19.33	12.55	234	14,040	9,120	1,579	1,025
B. N. C.	32	50.6	179	1.63	192	11,520	22.63	13.89	213	12,780	7,840	1,510	926
J. J. G.	21	50.2	164	1.53	175	10,500	20.62	13.49	203	12,180	7,960	1,425	931
E. J. W.	58	50.0	155	1.47	142	8,520	16.73	11.38	165	9,900	6,740	1,158	788
F. P.	17	49.3	161	1.50	188	11,280	22.18	14.75	229	13,740	9,160	1,591	1,061
V. E. H.	21	49.3	163	1.51	.157	9,420	18.50	12.26	198	11,880	7,870	1,365	904
T. M. C.	35	48.5	165	1.52	156	9,360	18.39	12.10	185	11,100	7,300	1,292	850
J. H.	26	45.5	154	1.40	153	9,180	18.03	12.89	173	10,380	7,415	1,223	874

RESULTS BY DECADES—MEN

SECOND DECADE

Name	Age	A			B′			C′			Deviation of CO_2 from cals. in per ct.	Deviation of O_2 from cals. in per ct.
		Gms. CO_2 per sq. m. per hr.	Deviation of CO_2 from average	Per cent deviation of CO_2	Cc. O_2 per hour per sq. m.	Deviation of O_2 from average	Per cent deviation of O_2	Cals. per sq. m. 24 hours	Deviation of cals. from average	Per cent deviation of cals.		
H. W.	19	15.82	+1.66	+11.7	8,914	+469	+ 5.6	1,053	+ 67	+ 6.8	+4.9	−1.2
M. H. K.	19	13.98	− .18	− 1.3	8,075	−370	− 4.4	949	− 37	− 3.8	+2.5	−0.6
F. M. M.	16	13.91	− .25	− 1.8	8,751	+306	+ 3.6	1,011	+ 25	+ 2.5	−4.3	+1.1
L. D. A.	19	13.27	− .89	− 6.3	7,900	−545	− 6.5	921	− 65	− 6.6	+0.3	+0.1
W. W. C.	17	14.17	+ .01	+ .08	8,385	− 70	− .8	980	− 6	− 0.6	+0.7	−0.2
C. H. H.	19	12.52	−1.64	−11.6	7,475	−970	−11.5	872	−114	−11.6	0.0	+0.1
V. G.	17	14.86	+ .70	+ 4.9	8,900	+455	+ 5.4	1,040	+ 54	+ 5.5	−0.6	−0.1
F. P.	17	14.75	+ .59	+ 4.2	9,160	+725	+ 8.6	1,061	+ 75	+ 7.6	−3.4	+1.0
Total	143	113.28			67,560			7,887				
Average	17.9	14.16			8,445			986				

THIRD DECADE

W. S.	22	14.29	+1.16	+ 8.8	8,840	+ 764	+ 9.5	1,029	+101	+10.8	− 2.0	−1.3
O. F. M.	24	12.46	− .67	− 5.1	8,030	− 46	− 0.6	922	− 16	− 1.7	− 3.4	+1.1
J. H. R.	23	13.84	+0.71	+ 5.4	8,174	+ 354	+ 4.4	956	+ 18	+ 1.9	+ 3.5	+2.5
D. H. W.	22	14.03	+0.90	+ 6.9	8,475	+ 399	+ 4.9	987	+ 49	+ 5.2	+ 1.7	−0.3
E. G.	20	15.09	+1.96	+14.9	8,970	+ 864	+10.7	1,053	+115	+12.3	+ 2.6	−1.6
W. A. M.	23	12.52	−0.61	− 4.6	7,860	− 216	− 2.7	907	− 31	− 3.3	− 1.3	+0.6
D. R. M.	28	12.95	−0.18	− 1.4	8,400	+ 324	+ 4.0	962	+ 24	+ 2.6	− 4.0	+1.4
M. B.	20	13.52	+0.39	+ 3.0	8,130	+ 54	+ 0.7	947	+ 9	+ 1.0	+ 2.0	−0.3
J. F. M.	20	13.73	+0.60	+ 4.6	8,280	+ 204	+ 2.5	963	+ 25	+ 2.7	+ 1.9	−0.2
W. J. T.	22	12.43	−0.70	− 5.3	7,875	− 201	− 2.5	908	− 21	− 2.2	− 3.1	−0.3
F. G. R.	20	14.87	+1.74	+13.3	8,300	+ 324	+ 4.0	992	+ 54	+ 5.8	+ 7.5	−1.8
C. D. R.	22	14.92	+1.79	+13.6	8,620	+ 544	+ 6.7	1,015	+ 77	+ 8.2	+ 5.4	−1.5
H. R. W.	24	13.85	+0.72	+ 5.5	8,380	+ 304	+ 3.8	974	+ 36	+ 3.8	+ 1.7	0.0
J. P. C.	23	11.85	−1.71	−13.0	7,070	−1,006	−12.5	825	−113	−12.0	− 1.0	−0.5
A. O. G.	25	11.92	−1.21	− 9.2	8,470	+ 394	+ 4.9	956	+ 18	+ 1.9	−11.1	+3.0
H. W. E.	23	12.23	−0.90	− 6.9	7,275	− 801	− 9.9	852	− 86	− 9.2	+ 2.3	−0.7
P. D. F.	23	13.83	+0.70	+ 5.3	8,320	+ 244	+ 3.0	968	+ 30	+ 3.2	+ 2.1	−0.2
C. B. S.	26	12.63	−0.53	− 4.0	7,440	− 636	− 7.9	899	− 39	− 4.2	+ 0.2	−3.7
J. H. H.	25	12.84	−0.29	− 2.2	7,752	− 324	− 4.0	903	− 35	− 3.7	+ 1.5	−0.3
B. A. W.	26	14.84	+1.71	+13.0	9,231	+1,149	+14.2	1,069	+131	+14.0	− 1.0	+0.2
H. H. A.	26	12.32	−0.81	− 6.2	7,675	− 401	− 5.0	889	− 49	− 5.2	− 1.0	+0.2
J. R.	27	12.82	−0.31	− 2.4	7,815	− 261	− 3.2	907	− 31	− 3.3	+ 0.9	+0.1
M. A. M.	29	13.42	+0.29	+ 2.2	8,025	− 51	− 0.6	937	− 1	− 0.1	+ 2.3	−0.5
F. P. R.	22	12.08	−1.05	− 8.0	7,480	− 596	− 7.4	867	− 71	− 7.6	− 0.4	+0.2
J. J. C.	27	12.49	−0.64	− 4.9	7,610	− 466	− 5.8	886	− 52	− 5.5	+ 0.6	−0.3

TABLE III—CONTINUED

Name	Age	A			B'			C'			Deviation of CO_2 from cals. in per ct.	Deviation of O_2 from cals. in per ct.
		Gms. CO_2 per sq. m. per hr.	Deviation of CO_2 from average	Per cent deviation of CO_2	Cc. O_2 per hour per sq. m.	Deviation of O_2 from average	Per cent deviation of O_2	Cals. per sq. m. 24 hours	Deviation of cals. from average	Per cent deviation of cals.		
E. H. T.	25	11.64	—1.49	—11.3	7,440	— 646	— 8.0	857	— 81	— 8.7	— 2.6	+0.7
P. M.	22	12.62	—0.51	— 3.9	8,225	+ 149	+ 1.8	944	+ 6	+ 0.6	— 4.5	+1.2
M. J. S.	24	13.22	+0.09	+ 0.7	8,170	+ 94	+ 1.2	947	+ 9	+ 1.0	— 0.3	+0.2
M. Y. B.	20	13.97	+0.84	+ 6.4	8,160	+ 84	+ 1.0	958	+ 30	+ 3.2	+ 3.2	—2.2
R. D. S.	21	13.88	+0.65	+ 5.0	7,860	— 216	— 2.7	930	— 8	— 0.9	+ 5.9	—1.8
R. G.	23	13.08	—0.05	— 0.4	7,780	— 296	— 3.7	908	— 30	— 3.2	+ 2.8	—0.5
V. R. B.	27	12.07	—1.06	— 8.1	7,540	— 536	— 6.6	872	— 66	— 7.1	— 1.0	+0.5
W. F. M.	21	14.48	+1.35	+10.3	8,640	+ 566	+ 7.0	1,009	+ 71	+ 7.6	+ 2.7	—0.6
H. H. A.	22	12.57	—0.56	— 4.3	7,610	— 466	— 5.8	886	— 52	— 5.6	+ 1.3	—0.2
H. C. B.	27	13.03	—0.10	— 0.7	8,240	+ 164	+ 2.0	950	+ 12	+ 1.3	— 2.1	+0.7
S. A. R.	23	12.35	—0.78	— 7.8	7,509	— 561	— 7.0	873	— 65	— 6.9	— 0.9	—0.1
W. G. J.	21	14.23	+1.10	+ 8.4	8,621	+ 539	+ 6.7	1,003	+ 65	+ 6.9	+ 1.5	—0.2
H. L. H.	26	13.71	+0.58	+ 4.4	8,560	+ 384	+ 4.8	985	+ 47	+ 5.0	— 0.6	—0.2
J. E. F.	21	13.87	+0.74	+ 5.6	7,990	— 86	— 1.1	940	+ 2	+ 0.2	+ 5.4	—1.3
J. K. M.	24	12.42	—0.71	— 5.4	7,730	— 346	— 4.3	895	— 43	— 4.6	— 0.8	+0.3
H. B. R.	25	12.13	—1.00	— 7.6	7,640	— 436	— 5.4	885	— 53	— 5.7	— 1.9	+0.3
J. B. T.	20	14.42	+1.29	+ 9.8	8,810	+ 734	+ 9.1	1,022	+ 84	+ 9.0	+ 0.8	+0.1
L. H. W.	27	12.34	—0.79	— 6.0	7,470	— 606	— 7.5	869	— 69	— 7.4	+ 1.4	—0.1
H. B. L.	20	13.02	—0.11	— 0.8	7,990	— 86	— 1.1	922	— 16	— 1.7	+ 0.9	+0.6
W. B. L.	29	11.77	+0.20	+ 1.5	7,670	— 406	— 5.0	879	— 59	— 6.3	+ 7.8	+1.3
H. Y.	22	13.32	+0.19	+ 1.4	8,250	+ 174	+ 2.2	955	+ 17	+ 1.8	— 0.4	+0.4
D. J. M.	20	13.04	—0.09	— 0.7	8,175	+ 99	+ 1.2	944	+ 6	+ .6	— 1.3	+0.6
E. T. W.	22	12.04	—1.09	— 8.3	7,650	— 426	— 5.3	881	— 77	— 8.2	— 0.1	+2.9
P. F. J.	20	13.87	+0.74	+ 5.6	8,480	+ 404	+ 5.0	985	+ 47	+ 5.0	+ 0.6	0.0
A. G. E.	26	13.93	+0.80	+ 6.1	7,850	— 226	— 2.8	928	— 10	— 1.1	+ 7.2	—1.7
R. I. C.	26	13.10	—0.03	— 0.2	8,370	+ 294	+ 3.6	964	+ 26	+ 2.8	— 3.0	+0.8
C. J. O.	27	.....	.....	.....	8,275	+ 199	+ 2.5	965	+ 27	+ 2.9	.....	.....
W. A. S.	21	13.65	+0.52	+ 4.0	8,160	+ 84	+ 1.0	952	+ 14	+ 1.5	+ 2.5	—0.5
J. C. C.	22	12.64	—0.49	— 3.7	7,870	— 206	— 2.6	912	— 26	— 2.8	— 0.9	+0.2
O. N. A.	25	12.83	—0.30	— 2.3	8,249	+ 173	+ 2.1	948	+ 10	+ 1.1	— 3.4	+1.0
I. A. F.	24	14.63	+1.50	+11.4	9,090	+1,014	+12.6	1,053	+115	+12.3	— 0.9	+0.3
A. F. G.	24	12.72	—0.41	— 3.1	7,525	— 551	— 6.8	881	— 57	— 6.1	+ 3.0	—0.7
M. B.	27	13.02	—0.11	— 0.8	8,182	+ 99	+ 1.2	945	+ 7	+ 0.7	— 1.5	+0.5
B. M. K.	27	12.55	—0.58	— 4.4	9,120	+1,044	+12.9	1,025	+ 87	+ 9.3	—13.7	+3.6
J. J. G.	21	13.49	+0.36	+ 2.7	7,960	— 116	— 1.4	931	— 7	— 0.7	+ 3.4	—0.7
V. E. H.	21	12.26	—0.87	— 6.6	7,870	— 206	— 2.6	904	— 34	— 3.6	— 3.0	+1.0
J. H.	26	12.89	—0.24	— 1.8	7,415	— 661	— 8.2	874	— 64	— 6.8	+ 5.0	—1.4
Total	1461	802.57			300,742			58,163				
Average	23.6	13.13			8,076			938				
FOURTH DECADE												
Prof. C.	36	12.17	— .72	— 5.6	7,370	— 345	— 4.5	857	— 43	— 4.8	— 0.8	+0.3
F. E. M.	38	13.53	+ .64	+ 5.0	7,980	+ 265	+ 3.4	932	+ 32	+ 3.6	+ 1.4	—0.2
F. A. R.	32	13.43	+ .54	+ 4.2	8,135	+ 420	+ 5.4	948	+ 48	+ 5.3	— 1.1	+0.1
N. K. W.	35	13.06	+ .17	+ 1.3	7,425	— 290	— 3.8	875	— 25	— 2.8	+ 4.1	—1.0
E. P. C.	35	10.88	—2.11	—16.4	7,001	— 714	— 9.2	805	— 95	—10.6	— 5.8	+1.4
W. F. B.	32	13.97	+1.08	+ 8.4	8,320	+ 605	+ 7.8	972	+ 72	+ 8.0	+ 0.4	—0.2
L. E. E.	31	13.93	+1.04	+ 8.1	8,490	+ 775	+10.0	987	+ 87	+ 9.7	— 1.6	+0.3
B. H.	39	11.32	—1.57	—12.2	6,930	— 785	—10.2	806	— 94	— 9.6	— 2.6	—0.6
H. F. T.	32	11.24	—1.65	—12.8	6,660	—1,055	—13.7	779	—121	—13.4	+ 0.6	—0.3
J. W. P.	30	14.33	+1.44	+11.2	8,730	+1,015	+13.2	1,017	+117	+13.0	— 1.8	+0.2
L. E. A.	30	13.89	+1.00	+ 7.8	8,115	+ 400	+ 5.2	952	+ 52	+ 5.8	+ 2.0	—0.6
B. N. C.	32	13.89	+1.00	+ 7.8	7,840	+ 125	+ 1.6	926	+ 26	+ 2.9	+ 4.9	—1.3
T. M. C.	35	12.10	—0.79	— 6.1	7,300	— 415	— 5.4	850	— 50	— 5.6	— 0.5	+0.2
Total	437	167.64			100,296			11,706				
Average	33.6	12.89			7,715			900				
FIFTH DECADE												
F. G. B.	41	12.47	+ .59	+ 5.0	7,551	+ 318	+ 4.3	879	+ 31	+ 3.6	+ 1.4	+0.7
A. L.	40	13.17	+1.01	+ 8.5	7,890	+ 488	+ 6.6	922	+ 66	+ 7.7	+ 0.8	—1.1
Dr. S.	43	10.25	—1.63	—13.7	6,580	— 822	—11.1	756	—100	—11.7	— 2.0	+0.6
Dr. P. R.	41	11.93	+ .05	+ 0.4	7,420	+ 18	+ 0.2	859	+ 3	+ 0.4	0.0	—0.2
Total	165	47.54			29,610			3,424				
Average	41.2	11.88			7,402			856				
SIXTH DECADE												
E. J. W.	58	11.38			6,740			788				
SEVENTH DECADE												
H. F.	63	11.19			7,449			851				

TABLE III—CONTINUED

NORMAL WOMEN

Name	Age	Weight in kgm.	Height in cm.	Body surface (DuBois)	A				B′			O′	
					CO_2 per min. (cc.)	CO_2 per hr. (cc.)	CO_2 per hour (gms.)	CO_2 per sq. m. per hour (gms.)	O_2 per min. (cc.)	O_2 per hr. (cc.)	O_2 per hour per sq. m. (cc.)	Calculated cals. (total 24 hours)	Cals. per sq. m. (24 hrs.)
Dr. M. D.	44	93.6	165	2.0	202	12,120	23.79	11.89	256	15,360	7,680	1,765	882.5
Miss O. A.	21	90.2	164	1.96	203	12,180	23.94	12.22	254	15,240	7,786	1,756	896.0
Miss H. H.	21	88.3	161	1.92	190	11,400	22.39	11.67	228	13,680	7,120	1,584	825.1
Mrs. H. D.	42	80.1	157	1.81	184	11,040	21.69	11.99	233	13,980	7,725	1,606	887.5
Miss C. Z.	39	67.2	170	1.78	176	10,560	20.75	11.65	220	13,200	7,410	1,521	854.9
Miss S.	27	65.5	171	1.77	178	10,680	20.98	11.85	202	12,120	6,840	1,426	805.1
Miss C. H.	25	63.4	166	1.71	156	9,360	18.39	10.75	207	12,420	7,260	1,413	827.0
Miss A. K.	23	63.2	171	1.75	165	9,900	19.44	11.13	202	12,120	6,925	1,402	801.0
Miss A. G.	21	63.0	161	1.67	153	9,180	18.04	10.82	192	11,520	6,895	1,324	792.5
Miss V. A.	21	62.9	168	1.72	167	10,020	19.68	11.44	188	11,280	6,552	1,324	770.0
Miss C.	22	61.9	168	1.70	177	10,620	20.83	12.26	203	12,180	7,165	1,427	839.0
Miss K. K.	21	61.5	154	1.59	....	.....	.....	.....	238	14,280	8,975	1,666	1,048
Dr. A. B.	32	60.3	163	1.65	197	11,820	23.21	14.08	207	12,420	7,525	1,486	901
Miss L. G.	38	59.5	159	1.61	134	8,040	15.83	9.84	173	10,380	6,448	1,187	737
Miss B. W.	22	59.4	162	1.63	180	10,800	21.20	13.02	223	13,380	8,210	1,546	947
Miss L. O.	23	59.3	169	1.68	176	10,560	20.75	12.35	207	12,420	7,400	1,448	862
Miss M. W.	25	58.6	167	1.65	168	10,080	19.79	11.99	206	13,360	7,485	1,429	865
Miss M. P.	28	58.1	168	1.66	170	10,200	20.03	12.07	222	13,320	8,020	1,518	914
Mrs. E. B.	53	58.0	163	1.63	171	10,260	20.16	12.36	202	12,120	7,435	1,415	867
Miss M. M.	18	57.9	164	1.63	191	11,460	22.50	13.81	207	12,420	7,615	1,475	904
Miss E. P.	23	57.7	175	1.70	166	9,960	19.60	11.53	207	12,420	7,310	1,430	841
Miss L. K.	22	56.8	166	1.63	153	9,180	18.04	11.07	199	11,940	7,325	1,365	838
Miss E. A.	15	56.8	157	1.56	205	12,300	24.18	15.49	231	13,860	8,880	1,630	1,044
Miss A. M.	20	56.8	152	1.52	155	9,300	18.24	12.01	192	11,520	7,575	1,329	873
Miss J. C.	22	55.1	162	1.58	157	9,420	18.52	11.72	198	11,880	7,520	1,363	862
Miss G. L.	21	55.0(?)	166	1.61	173	10,380	20.39	12.66	214	12,840	7,970	1,480	919
Mrs. D. C.	36	54.9	153	1.51	160	9,600	18.86	12.49	182	10,920	7,230	1,278	845
Miss M. T.	20	54.5	164	1.58	147	8,820	17.35	10.98	196	11,760	7,440	1,359	859
Miss F. K.	18	54.1	164	1.58	157	9,420	18.52	11.72	179	10,740	6,800	1,262	798
Miss J. N. B.	26	53.8	160	1.55	134	8,040	15.81	10.19	178	10,680	6,885	1,215	784
Miss L. T.	31	53.6	155	1.51	152	9,120	17.95	11.89	178	10,680	7,070	1,247	825
Miss F. E.	22	53.1	162	1.56	161	9,660	19.00	12.18	202	12,120	7,770	1,391	892
Miss L.	25	52.4	168	1.58	162	9,720	19.12	12.09	188	11,280	7,140	1,321	836
Miss A. D.	37	52.3	166	1.57	159	9,540	18.78	11.97	196	11,760	7,485	1,355	863
Miss B.	21	52.2	158	1.52	173	10,380	20.39	13.42	202	12,120	7,970	1,409	926
Miss R. M.	16	52.1	162	1.54	159	9,540	18.78	12.21	195	11,700	7,590	1,353	879
Miss L. J.	24	51.8	159	1.52	142	8,520	16.77	11.03	179	10,740	7,070	1,235	812
Mrs. A.	29	51.6	163	1.54	166	9,960	19.60	12.73	205	12,300	7,980	1,421	922
Miss J. M.	16	51.4	158	1.50	....	.....	.....	.....	220	13,200	8,795	1,541	1,028
Miss J. B.	27	51.1	163	1.53	146	8,760	17.23	11.27	183	10,980	7,175	1,265	827
Miss R. A.	21	50.8	155	1.47	161	9,660	19.00	12.92	184	11,040	7,510	1,296	881
Miss M. C.	16	50.6	162	1.52	145	8,700	17.11	11.26	185	11,100	7,300	1,273	838
Miss E. C.	25	50.5	164	1.53	155	9,300	18.24	11.93	192	11,520	7,525	1,327	867
Miss I. B.	18	50.1	166	1.55	160	9,600	18.86	12.17	173	10,380	6,700	1,235	797
Miss E. S.	25	50.0	164	1.53	154	9,240	18.19	11.89	195	11,700	7,647	1,345	879
Miss C. B.	24	49.8	162	1.51	168	10,080	19.79	13.10	205	12,300	8,140	1,408	932
Miss G. V.	22	49.7	160	1.50	128	7,680	15.12	10.09	166	9,960	6,645	1,139	759
Miss D. W.	19	49.4	160	1.50	153	9,180	18.03	12.03	187	11,220	7,475	1,300	866
Miss M. H.	27	49.1	151	1.43	135	8,100	15.95	11.15	171	10,260	7,170	1,178	823
Miss C. L.	21	49.1	151	1.43	153	9,180	18.03	12.62	195	11,700	8,175	1,341	938
Miss C. E.	74	48.9	164	1.52	122	7,320	14.40	9.47	160	9,600	6,320	1,095	721
Miss V. M.	24	48.9	162	1.50	149	8,940	17.59	11.72	198	11,880	7,915	1,351	902
Miss M. S.	24	48.5	159	1.48	167	10,020	19.68	13.29	216	12,960	8,751	1,480	1,000
Miss G. F.	27	48.5	155	1.45	140	8,400	16.53	11.41	180	10,800	7,445	1,233	852
Miss K. M.	22	48.2	161	1.49	161	9,660	19.00	12.75	184	11,040	7,415	1,294	868
Miss L. B.	27	47.0	167	1.50	136	8,160	16.05	10.71	169	10,140	6,770	1,168	778
Miss E. T.	22	46.7	164	1.48	151	9,060	17.79	12.02	195	11,700	7,900	1,336	902
Miss H. T.	25	45.0	159	1.43	156	9,360	18.40	12.87	203	12,180	8,515	1,393	974
Miss R. W.	21	45.0(?)	153	1.39	141	8,460	16.65	11.98	186	11,160	8,025	1,273	916
Mrs. A. L.	29	44.9	159	1.43	147	8,820	17.35	12.13	184	11,040	7,720	1,272	889
Miss M. J.	27	44.8	157	1.42	137	8,220	16.18	11.40	172	10,320	7,270	1,189	837
Miss J.	24	43.0	159	1.41	139	8,340	16.41	11.64	165	9,900	7,020	1,158	821
Miss A. C.	38	42.6	165	1.44	138	8,280	16.30	11.32	168	10,080	6,995	1,168	811
Miss D. A.	19	41.5	154	1.35	136	8,160	16.05	11.89	176	10,560	7,820	1,207	893
Miss E. W.	24	40.5	157	1.35	153	9,180	18.03	13.37	183	10,980	8,130	1,275	944
Miss J. T.	36	40.0	168	1.42	139	8,340	16.41	11.57	186	11,160	7,855	1,269	892
Mrs. S. C.	52	37.4	155	1.29	122	7,320	14.39	11.15	140	8,400	6,515	1,013	786
Mrs. A. A.	43	35.6	170	1.35	119	7,140	14.04	10.41	169	10,140	7,515	1,141	844

TABLE III—Continued

Results by Decades—Women

SECOND DECADE

Name	Age	A			B′			C′			Deviation of CO_2 from cals. in per cent	Deviation of O_2 from cals. in per cent
		Gms. CO_2 per sq. m. per hr.	Deviation of CO_2 from average	Per cent deviation of CO_2	Cc. O_2 per hour per sq. m.	Deviation of O_2 from average	Per cent deviation of O_2	Cals. per sq. m. (24 hours)	Deviation of cals. from average	Per cent deviation of cals.		
Miss M. M.	18	13.81	+1.24	+ 9.9	7,615	+ 93	— 1.2	904	+ 27	+ 3.1	+6.8	—4.3
Miss E. A.	15	15.49	+2.92	+23.2	8,880	+1,358	+18.00	1,044	+167	+19.1	+4.1	—1.1
Miss F. K.	18	11.72	—0.85	— 6.8	6,800	— 722	— 9.6	798	— 79	— 9.0	+2.2	—0.6
Miss R. M.	16	12.21	—0.36	— 2.9	7,590	+ 68	— 0.9	879	+ 2	+ 0.2	—3.1	—1.1
Miss J. M.	16	.....	.....	.....	(8,795)	.....	.....	(1,028)	.....	.....	.....	.....
Miss M. C.	16	11.26	—1.31	—10.4	7,300	— 222	— 3.0	838	— 39	— 4.4	—6.0	+1.4
Miss I. B.	18	12.17	—0.40	— 3.2	6,700	— 822	—10.9	797	— 80	— 9.0	+5.8	—1.9
Miss D. W.	19	12.03	—0.54	— 4.3	7,475	— 47	— 0·6	866	— 11	— 1.3	—3.0	+0.7
Miss D. A.	19	11.89	—0.68	— 5.4	7,820	+ 298	+ 4.0	893	+ 16	+ 1.8	—7.2	+2.2
Total	155	100.58			60,180			7,019				
Average	17.2	12.57			7,522			877				

THIRD DECADE

Miss O. A.	21	12.22	+ 33	+ 2.8	7,786	+ 275	+ 3.7	896	+ 30	+ 3.5	—0.7	+0.2
Miss H. H.	21	11.67	— 22	— 1.9	7,120	— 391	— 5.2	825	— 41	— 4.7	+2.6	—0.5
Miss S.	27	11.85	— 4	— 0.3	6,840	— 671	— 9.0	805	— 61	— 7.0	+6.7	—2.0
Miss C. H.	25	10.75	—114	— 9.6	7,260	— 251	— 3.4	827	— 39	— 4.5	—5.1	+1.1
Miss A. K.	23	11.13	— 76	— 6.4	6,925	— 586	— 7.8	801	— 65	— 7.5	+1.1	—0.3
Miss A. G.	21	10.82	—107	— 9.0	6,895	— 616	— 8.2	792	— 74	— 8.5	—0.5	+0.3
Miss V. A.	21	11.44	— 45	— 3.8	6,552	— 959	—12.8	770	— 96	—11.1	+7.3	—1.7
Miss C.	22	12.26	+ 37	+ 3.1	7,165	— 346	— 4.6	839	— 27	— 3.1	+6.2	—1.5
Miss B. W.	22	13.02	+113	+ 9.5	8,210	+ 699	+ 9.3	947	+ 81	+ 9.4	+0.1	—0.1
Miss L. B.	23	12.35	+ 46	+ 3.9	7,400	— 111	— 1.5	862	— 4	— 0.5	+4.4	—1.0
Miss M. W.	25	11.99	+ 10	+ 0.8	7,485	— 26	— 0.35	865	— 1	— 0.1	+0.9	—2.5
Miss M. P.	28	12.07	+ 18	+ 1.5	8,020	+ 509	+ 6.8	914	+ 48	+ 5.6	—4.1	+1.2
Miss E. P.	23	11.53	— 36	— 3.0	7,310	— 201	— 2.7	841	— 25	— 2.9	—0.1	+0.2
Miss L. K.	22	11.07	— 82	— 6.9	7,325	— 186	— 2.5	838	— 28	— 3.2	—3.7	+0.7
Miss A. M.	20	12.01	+ 12	+ 1.1	7,575	+ 64	+ 0.9	873	+ 7	+ 0.8	+0.3	+0.1
Miss J. C.	22	11.72	— 17	— 1.4	7,520	+ 9	+ 0.1	862	— 4	— 0.5	—0.9	+0.6
Miss G. L.	21	12.66	+ 77	+ 6.5	7,970	+ 459	+ 6.1	919	+ 53	+ 6.1	+0.4	±0.0
Miss M. T.	20	10.98	— 91	— 7.7	7,440	— 71	— 0.9	859	— 7	— 0.8	—6.9	—0.1
Miss J. N. B.	26	10.19	—170	—14.3	6,885	— 626	— 8.4	784	— 82	— 9.5	—4.8	+1.1
Miss F. E.	22	12.18	+ 29	+ 2.5	7,770	+ 259	+ 3.6	892	+ 26	+ 3.0	—0.5	+0.6
Miss L.	25	12.09	+ 20	+ 1.7	7,140	— 371	— 5.0	836	— 30	— 3.5	+5.2	—1.5
Miss B.	21	13.42	+153	+12.9	7,970	+ 459	+ 6.1	926	+ 60	+ 7.0	+5.9	—0.9
Miss L. J.	24	11.03	— 86	— 7.2	7,070	— 441	— 5.9	812	— 54	— 6.2	—1.0	+0.3
Mrs. A.	29	12.73	+ 84	+ 7.1	7,980	+ 469	+ 6.3	922	+ 56	+ 6.5	+0.6	—0.2
Miss J. B.	27	11.27	— 62	— 5.2	7,175	— 336	— 4.5	827	— 39	— 4.5	—0.7	±0.0
Miss R. A.	21	12.92	+103	+ 8.7	7,510	— 1	± 0.0	881	+ 15	+ 1.7	+7.0	—1.7
Miss E. C.	25	11.93	+ 4	+ 0.3	7,525	+ 14	+ 0.2	867	+ 1	+ 0.1	+0.2	+0.1
Miss E. S.	25	11.89	.....	.....	7,647	+ 136	— 7.0	879	+ 13	+ 1.5	—1.5	—8.5
Miss C. B.	24	13.10	+121	+10.2	8,140	+ 629	+ 8.4	932	+ 66	+ 7.6	+2.6	+0.8
Miss G. J.	22	10.09	—180	—15.1	6,645	— 866	—11.5	759	—107	—12.4	—2.7	+0.9
Miss M. H.	27	11.15	— 74	— 6.2	7,170	— 341	— 4.6	823	— 43	— 5.0	—1.2	+0.4
Miss C. L.	21	12.62	+ 73	+ 6.1	8,175	+ 664	+ 8.9	938	+ 72	+ 8.3	—2.2	+0.6
Miss V. M.	24	11.72	— 17	— 1.4	7,915	+ 404	+ 5.4	902	+ 36	+ 4.2	—5.6	+1.2
Miss M. S.	24	13.29	+140	+11.8	8,751	+1,240	+16.6	1,000	+134	+15.5	—3.7	+1.1
Miss G. F.	27	11.41	— 48	— 4.0	7,445	— 66	— 0.9	852	— 14	— 1.6	—2.4	+0.7
Miss K. M.	22	12.75	+ 86	+ 7.2	7,415	— 96	— 1.3	868	+ 2	+ 0.2	+7.0	—1.5
Miss L. B.	27	10.71	—118	— 9.9	6,770	— 741	— 9.9	778	— 88	—10.2	+0.3	+0.3
Miss E. T.	22	12.02	+ 13	+ 1.1	7,900	+ 389	+ 5.2	902	+ 36	+ 4.2	—3.1	+1.0
Miss H. T.	25	12.87	+ 98	+ 8.3	8,515	+1,004	+13.4	974	+108	+15.5	—4.2	+0.9
Miss R. W.	21	11.98	+ 9	+ 0.8	8,025	+ 514	+ 6.9	916	+ 50	+ 5.8	—5.0	+1.1
Mrs A. L.	29	12.13	+ 24	+ 2.0	7,720	+ 209	+ 2.8	889	+ 23	+ 2.7	—0.7	+0.1
Miss M. J.	27	11.40	— 49	— 4.1	7,270	— 241	— 3.2	837	— 29	— 3.4	—0.7	+0.2
Miss J.	24	11.64	— 25	— 2.1	7,020	— 491	— 6.6	821	— 45	— 5.2	+3.1	—1.4
Miss E. W.	24	13.37	+148	+12.5	8,130	+ 619	+ 8.3	944	+ 78	+ 9.0	+3.5	—0.7
Total	1,042	52,344			330,476			38,096				
Average	23.7	11.89			7,511			866				

FOURTH DECADE

Miss C. Z.	39	11.65	—0.20	— 1.7	7,410	+158	+ 2.2	855	+ 14	+ 1.7	— 3.4	+0.5
Dr. A. B.	32	14.08	+2.23	+18.8	7,525	+273	+ 3.8	901	+ 60	+ 7.1	+11.7	+3.3
Miss L. G.	38	9.84	—2.01	—17.0	6,448	—804	—11.1	737	—104	—12.4	— 4.6	+1.3
Mrs. D. C.	36	12.49	+0.64	+ 5.4	7,230	— 22	— 0.3	845	+ 4	+ 0.5	+ 4.9	—0.8
Miss L. T.	31	11.89	+0.04	+ 0.3	7,070	—182	— 2.5	825	— 16	— 1.9	+ 2.2	—0.6
Miss A. D.	37	11.97	+0.12	+ 1.0	7,485	+233	+ 3.2	863	+ 22	+ 2.6	— 1.6	+0.6
Miss A. C.	38	11.32	—0.53	— 4.5	6,995	—257	— 3.5	811	— 30	— 3.6	— 0.9	+0.1
Miss J. T.	36	11.57	—0.28	— 2.4	7,855	+603	+ 8.3	892	+ 51	+ 6.1	— 8.5	+2.2
Total	287	94.81			58,018			6,729				
Average	35.9	11.85			7,252			841				

TABLE III—CONTINUED

Name	Age	A: Gms. CO_2 per sq. m. per hour	A: Deviation of CO_2 from average	A: Per cent deviation of CO_2	B′: Cc. O_2 per hour per sq. m.	B′: Deviation of O_2 from average	B′: Per cent deviation of O_2	C′: Cals. per sq. m. (24 hours)	C′: Deviation of cals. from average	C′: Per cent deviation of cals.	Deviation of CO_2 from cals. in per ct.	Deviation of O_2 from cals. in per ct.
FIFTH DECADE												
Dr. M. D.	44	11.89	+0.46	+4.0	7,680	+ 40	+0.5	883	+11	+1.3	+2.7	—0.8
Mrs. H. D.	42	11.99	+0.56	+4.9	7,725	+ 85	+1.1	888	+16	+1.8	+5.1	—0.7
Mrs. A. A.	43	10.41	—1.02	—8.9	7,515	—125	—1.6	844	—28	—3.2	—5.7	+1.6
Total	129	34.29			22,920			2,615				
Average	43	11.43			7,640			872				
SIXTH DECADE												
Mrs. E. B.	53	12.36	+0.60	+5.1	7,435	+460	+6.6	867	+41	+5.0	+0.1	+1.6
Mrs. S. C.	52	11.15	—0.61	—5.1	6,515	—460	—6.6	786	—40	—5.0	—0.1	—1.6
Total	105	23.51			13,950			1,653				
Average	52.5	11.76			6,975			826				
SEVENTH DECADE												
Miss C. E.	74	9.47	.....	.....	6,320	.....	.....	721	....	.....	.....	.....

CO_2 elimination in a large number of normal individuals. This scale is shown later in this paper and is seen to correspond closely with the scale constructed by the writer. The only significant discrepancies between the two scales occur in the upper decades. It happens, however, that the bulk of subjects studied by Benedict and his associates fell by age into the lower decades, making the figures for these decades more significant. It is probable that the scale computed by the writer, which follows the curve constructed by Aub and DuBois,[8] is somewhat nearer the actual average for the upper decades.

We have not attempted to draw conclusions from Table III as to the correlation of the O_2 and CO_2 figures, respectively, with the calories, inasmuch as the calories are calculated calories (indirect method) and not measured calories (direct method). It is seen at a glance, however, that the calorie figures follow the O_2 figures more closely than they follow the CO_2 figures. It is, therefore, obvious that the practical result of the customary method of deriving calories from O_2 and CO_2 figures is that the O_2 figure is more influential in determining the resultant calorie figures than the CO_2 figures are.

To make our figures of more value we requested Dr. Pearl to make a statistical review of them, and are indebted to him for the following:

MEMORANDUM RE CALORIMETRY

The point at issue is whether CO_2 output may be used as a basis of calorie calculation with as much validity as attached to the use of O_2 intake for the same purpose.

To test the point adequately it is necessary to determine: (a) whether on the same material the variation of the CO_2 figures significantly differs from the variation of the O_2 figures, and (b) whether on the same material there is any significant difference between O_2 intake and CO_2 output in respect of the degree of their correlation with calories per square meter.

The significant figures in question (a) will be coefficients of variation rather than standard deviations, because of different units involved, and because it is *relative* rather than absolute variability in which we are interested.

Table 1 furnishes the needed constants for each of the four series of original data. A standard deviation is denoted by σ and a coefficient of variation by V.

Let subscript letters have the following significance:

A = CO_2 per $(M)^2$ per hour in grams.
B = O_2 per $(M)^2$ per hour in grams.
C = Calories per $(M)^2$ per hour.
B′ = O_2 per $(M)^2$ per hour in c. c.
C′ = Calories per $(M)^2$ per 24 hours.

The significant comparisons in respect of variability are:

Direct calorimetry (10 cases)

$V_A - V_B = 7.22 - 12.93 = -5.71 \pm 2.26$ Diff/P.E.$_{Diff} = 2.5$.

Direct calorimetry (17 cases)

$V_A - V_B = 10.50 - 10.40 = + .10 \pm 1.73$ Diff/P.E.$_{Diff} = .06$.

Normal men

$V_A - V_B = 7.94 - 7.07 = + .87 \pm .54$ Diff/P.E.$_{Diff} = 1.6$.

Normal women

$V_A - V_B = 8.37 - 7.06 = +1.31 \pm .65$ Diff/P.E.$_{Diff} = 2.0$.

From these figures we conclude that:

1. There is no significant difference in relative variability, in any of the four series, between O_2 intake and CO_2 output.

[8] Aub and DuBois: The Basal Metabolism of Old Men. Arch. Int. Med., 1917, XVIII, 823.

TABLE 1

	CO_2 per sq. m. per hr. (Gms.) = A	O_2 per sq. m. per hr. (Gms.) = B	Cals. per sq. m. per hr. = C	O_2 per sq. m. per hr. (cc.) = B′	Cals. per sq. m. 24 hrs. = C′
Direct calorimetry (10 cases): mean	+14.08± .22	+12.20± .34	+44.87± .77		
Direct calorimetry (10 cases): σ	1.02± .15	1.58± .24	3.61± .54		
Direct calorimetry (10 cases): V	7.22±1.09	12.93±1.98	8.04±1.22		
Direct calorimetry (17 cases): mean	13.21± .23	11.95± .20	38.07± .74		
Direct calorimetry (17 cases): σ	1.39± .16	1.24± .14	4.53± .52		
Direct calorimetry (17 cases): V	10.50±1.23	10.40±1.22	11.89±1.40		
Indirect calorimetry (17 cases): mean	*	*	+38.47± .58		
Indirect calorimetry (17 cases): σ	*	*	3.56± .41		
Indirect calorimetry (17 cases): V	*	*	9.25±1.08		
Normal men: mean	+13.10± .08			+7995.45±40.65	931.53±4.72
Normal men: σ	1.04± .05			565.42±28.75	65.71±3.34
Normal men: V	7.94± .41			7.07± .36	7.05± .36
Normal women: mean	+11.90± .08			7454.55±43.69	861.36±4.72
Normal women: σ	1.00± .06			526.28±30.90	56.89±3.34
Normal women: V	8.37± .51			7.06.00± .42	6.61± .39

* Omitted because identical with immediately preceding group in same columns.

The former is certainly not less variable than the latter, having regard to the probable error. The ratio of the difference in variability to its probable error is in no case greater than 2.5, a value too small to attach any significance to.

2. While in the last three series the sign of the difference is positive, indicating a greater variability of the CO_2 determination as compared with the O_2, the differences are so small in magnitude as not to differ significantly from zero.

Turning to the second question, the pertinent correlation coefficients are given in Table 2. In this table r denotes a coefficient of correlation between the two variables indicated by the attached subscript letters.

TABLE 2

	Direct calorimetry (10 cases)	Direct calorimetry (17 cases)
r_{AC}	+ .719± .103	+ .846± .047
r_{BC}	+ .488± .162	+ .836± .049

The significant comparisons are:

Direct calorimetry (10 cases)

$r_{AC} - r_{BC} = .719 - .488 = + .231 \pm .192$ Diff/P.E.$_{Diff} = 1.2$.

Direct calorimetry (17 cases)

$r_{AC} - r_{BC} = .846 - .836 = - .010 \pm .068$ Diff/P.E.$_{Diff} = 0.1$.

From these results it must be concluded that the O_2 intake is not significantly more highly correlated with directly measured calorie output than is CO_2. The differences in the correlations are sensibly zero, having regard for these probable errors. In the longer series (17 cases) the correlation is actually slightly (but not significantly) higher for the CO_2 with calories than for the O_2 with calories.

Method for Measuring Carbon-Dioxide

With the foregoing considerations in mind, it seemed reasonable to construct an apparatus for collecting and measuring carbon-dioxide elimination, with a view toward its possible use as a clinical index to the metabolic rate.

Such an apparatus is shown in Fig. 1, and is quite simple. The method is "open," the older U. S. Army gas-mask being used to deliver outside air to the subject and to carry expired air to the tubing leading to the three jars. The gas-mask canister, seen hanging from the horizontal bar, was emptied by removing the valve in the bottom, removing the contents and sealing the valve into place again. On the intake side, then, there is nothing between the patient and the outside air except a light rubber valve in the bottom of the canister, which rises and falls with respiration.*

Expired air passes through the "flutter" valve of the gas-mask and is caught in a rubber cuff, that is sealed with paraffin about this outlet valve. The cuff tapers into rubber tubing and the expired air passes through the three collecting jars.

Resistance to the passage of air through the jars has been measured by inserting a water manometer between the subject and the first jar. Observations upon two large men showed an average momentary rise of pressure of 6 to 8 mm. H_2O. On deep respiration the pressure rose occasionally with a quick elevation, such as one sees in a "water hammer" pulse, to 14 mm. H_2O. Such pressure changes, it was thought, made a fan superfluous. There is no inspiratory effort whatever.

The three jars are identical in construction and are such as were part of the original Benedict "portable" apparatus.

* The mouth-piece of the gas-mask is too small for this work and the larger mouth-piece made by the Sanborn Company, Boston, Mass., is used. It is removed and boiled for each test.

FIG. 1.—Apparatus and Balance for Measuring Carbon-Dioxide Elimination.

Incoming air is carried through a tube almost to the bottom of the jar. Here it is scattered through a cone with multiple perforations, filters upward through the chemicals, and passes out at the top.

The first jar contains 4-mesh calcium chloride.[10] This has been found to desiccate expired air completely.

The second jar contains soda lime and absorbs carbon-dioxide from the dried air. Observations have been made upon the efficacy of this soda lime in repeated tests by attaching a soda lime and calcium chloride jar at the end of the usual series of three jars. It was found that the soda lime jar, after it has absorbed as much as 111 grms. CO_2 still completely removed CO_2 from the air. The writer breathed through the jars for 15 minutes after the soda lime had absorbed 111 grms. CO_2. He had not been prepared, was not quiet and his CO_2 output was 39 per cent above the average normal. No CO_2 was collected in the additional jars. CO_2 did, however, pass through the absorbing jars after 150 grms. CO_2 had been absorbed. To be perfectly safe we have become accustomed to change soda lime after it has taken up a total of 75 grms.[11]

The third jar contains calcium chloride of the same type as that used in the first jar. This third jar is necessary because the soda lime (jar II) contains a rather high percentage of moisture, some of which is carried out of jar II during each test; jar III absorbs this vapor. This increase in weight in jar III, therefore, must be added to the net increase in weight of jar II in order that the determination of CO_2 may be correct.

Technic of Test

The patient is prepared in the usual way, by the omission of breakfast and by half an hour's rest before the test. The room is well ventilated before and during the examination. The patient is carefully protected from cold.

The mouth-piece and nose-clip[12] are adjusted. The patient is instructed to be quiet and to breathe naturally. For several minutes a preliminary period is carried out, the patient breathing through the first jar only. This is done in order to allow the patient to become accustomed to the procedure, and the length of this preliminary period depends upon the readiness with which he settles down to the task. It is found that most complaints arise during the very beginning of the test. If a new start must be made, it is, therefore, usually accomplished during this preliminary period, and it is not necessary to reweigh jars II and III. As soon as the patient is quiet and breathing smoothly, jars II and III, which have been previously attached to each other, are joined to jar I, note being taken of the time—to the second. The expired air is passed through all these jars for ten minutes. Ten-minute periods are repeated until two of the results agree reasonably closely. The sum of the increase in weight in jars II and III represents the CO_2 elimination. The CO_2 for two periods is added and multiplied by 3. This gives CO_2 elimination per hour. This is divided by the body surface (DuBois Height-Weight Chart)[13]. The resultant figure—grms. CO_2 per sq. meter per hour—is our end result. This is compared with the standard normal figures and the percentage deviation from the average normal figure is calculated.

TABLE IV

THE CARBON-DIOXIDE ELIMINATION OF HEALTHY MEN AT REST (POST-ABSORPTIVE PERIOD)

THE AUTHOR'S NORMAL CONTROL OBSERVATIONS

3rd and 4th Decades

Name	Age	Height in cm.	Weight in kgm.	Body surface (Dubois formula)	A		Deviation of CO_2 from average (gms.)	Percent deviation of CO_2 from average
					CO_2 eliminated per hr. in gms.	CO_2 per hr. per sq. m. body surface (gms.)		
N. C.	33	180	75.9	1.95	23.88	12.25	—0.58	— 4.7
W. R.	25	180	73.2	1.925	24.08	12.51	—0.32	— 2.5
C. P.	28	177	71.4	1.87	23.25	12.43	—0.40	— 3.1
W. L.	33	178	72.7	1.90	23.40	12.32	—0.51	— 3.9
L. G.	27	179	61.4	1.77	21.36	12.07	—0.76	— 5.9
S. S.	25	172	66.4	1.78	22.76	12.79	—0.04	— 0.3
L. M.	26	190	81.8	2.09	27.96	13.38	+0.55	+ 4.3
V. M.	30	178	72.3	1.89	22.44	11.87	—0.96	— 8.1
J. K.	22	170	51.82	1.58	22.08	13.98	+1.15	+ 8.9
D. A.	29	175	60.5	1.74	25.64	14.74	+1.91	+14.9
G. G.	22	188	84.09	2.11	31.04	14.71	+1.88	+14.7
H. R.	29	177	65.9	1.81	23.40	12.93	+0.10	+ 0.8
H. J.	27	182	70.5	1.90	22.64	11.92	—0.91	— 7.1
G. H.	29	173	65.4	1.78	21.24	11.93	—0.90	— 7.0
P. C.	27	173	57.7	1.69	22.12	13.09	+0.26	+ 2.0
W. T.	27	168	62.5	1.72	20.80	12.09	—0.74	— 5.8
E. B.	30	185.5	76.3	1.99	26.24	13.19	+0.36	+ 2.8
Total	469					218.20		
Average	27.6					12.83		

Application of the Method

In order to test the method which has just been described a series of 17 observations was made upon normal subjects. Each observation included a preliminary period and 15 minutes of CO_2 collection. The results are shown in Table IV. The table shows that an average of 12.83 grms. CO_2 per square meter of body surface per hour is eliminated by healthy men whose ages lie between 20 and 40 years.

On the basis of this standard figure, a prediction was made by the writer of CO_2 elimination for various ages and for both sexes. This is tabulated in Table IV. These results are based upon the curve constructed by Aub and DuBois,[14] showing the heat production of healthy males at various ages. The figures for women were obtained by deducting 7 per cent from the figures for men. These predicted values are shown in Table V, side by side with the actual values observed by Benedict and his associates—obtained from the analysis of Benedict's figures by decades (Table III). The correlation between the two sets of figures will be seen to be close for the decades in which actual observations were made: those of

[10] Cacl, 4 mesh, purified, anhydrous, for drying purposes, purchased from J. T. Baker Chem. Co., Phillipsburg, N. J., in 5-pound jars.

[11] The soda lime used is the Wilson [navy] soda lime, purchased from the Dewey and Almy Chemical Co., N. Cambridge, Mass., in 45-pound cans. Professor Wilson, of the Massachusetts Institute of Technology, writes me that this soda lime is by far the most active preparation that is available for CO_2 absorbing purposes.

[12] The gas-mask nose-clip is excellent.

[13] Lusk: Science of Nutrition. W. B. Saunders Co., Philadelphia and London, 1919.

[14] *Loc. cit.*

Benedict and others are 13.13 grms. and 12.89 grms. for the third and fourth decades, respectively. The author's figure for the third and fourth decades together is 12.83 grms. A reasonably close correlation exists throughout the figures for women, again especially in the lower decades. The figures of the upper decades of man show discrepancies which may be explained by pointing out the relatively small number of observations by Benedict and others that fell within the upper decades.

TABLE V

NORMAL STANDARDS OF CARBON-DIOXIDE ELIMINATION

Figures Represent Gms. CO_2 per Sq. Meter Body Surface (DuBois Formula) per Hour *

Age	Men			Women		
	Benedict, Emmes, Roth and Smith	The author	Average	Benedict, Emmes, Roth and Smith	The author	Average
15–20	14.16	13.90	14.03	12.57	12.93	12.75
20–30	13.13	12 83	12.98	11.89	12.02	11.95
30–40	12.89	12.83	12.86	11.85	11.86	11.85
40–50	11.88	12.52	12.20	11.43	11.74	11.58
50–60	11.38	12.21	11.79	11.76	11.37	11.56
60–70	11.19	11.86	11.52	.....	11.05	11.05
70–80	.....	11.53	11.53	9.47	10.71	10.14

PROPOSED SCALE OF NORMAL FIGURES

Age	Men	Women
15–20	14.03	12.75
20–30	12.98	11.95
30–40	12.86	11.85
40–50	12.52	11.74
50–60	12.21	11.37
60–70	11.86	11.05
70–80	11.53	10.71

* The author's standard figures were calculated from the findings on the 17 normal controls between 20 and 40 years. From these figures the expected CO_2 elimination for men and women at various ages was computed from the chart by Aub and DuBois,† showing metabolic rates at various ages.

† The Basal Metabolism of Old Men. Aub and DuBois. Arch. Int. Med., 1917, V. 19, Part ii.

A satisfactory scale of normal figures may therefore be obtained by taking an average between Benedict's and the author's figures for the lower decades. For decades above the fourth it seems to me safer to follow the CO_2 figures predicated upon the curve of Aub and DuBois. Such a proposed scale is shown at the bottom of Table V. It must be remembered, however, that considerable deviation from such figures must be expected, even in normal subjects, as shown by the Benedict reports of actual observations.

DISCUSSION

EFFECT OF SUPERVENTILATION OF THE LUNGS

It is generally believed by those interested in the study of gas exchange that CO_2 is eliminated in a manner less even than the absorption of O_2. We have considered this matter carefully and have obtained the following data.

It has been shown from the analysis of the 27 experiments with subjects in the chamber calorimeter that the co-efficient of correlation of CO_2 with calories is actually higher than that of O_2 with calories. So far, then, as this points the way, we may say that CO_2 furnishes a better index to the heat production (basal metabolism) than does O_2—that is, under ideal conditions. It also seems fair to say that, if any handicap in favor of CO_2 as an index to basal metabolism is found to exist under ideal conditions, then such a handicap must still be considered to play some rôle even under less favorable conditions.

Lusk, in the introduction of his *Science of Nutrition*,[15] quotes experiments of Lossen upon the CO_2 elimination during extreme variations of ventilation of the lungs. The subject voluntarily breathed at various rates between 75 and 182 liters of air per 15 minutes. The results showed that CO_2 elimination for 15-minute periods could not be altered by the rate of ventilation of the lungs except in so far as it might be raised by excessive activity of the respiratory muscles.

Let us consider the theoretical aspect. It is generally believed that respiration is caused by the circulation of CO_2 through the respiratory center, and that the absorption of O_2 is a purely passive act. Inasmuch as the act of gas exchange is caused by the CO_2 that results from oxidation and not by a demand for O_2, might we not assume that CO_2 elimination should be closely related in a quantitative way to heat production?

It remains, however, to investigate the CO_2 elimination during tests by the "indirect" method. The question is whether patients breathing through their mouths, with their nostrils closed, breathe so unnaturally as to "wash out" CO_2 that has previously been formed in the body, and so give a false index to the actual CO_2 formation and hence to the heat production. This can best be answered by actual tests. If CO_2 can be "washed out" by a nervous subject and O_2 not absorbed in a proportionate amount, then a handicap can be shown in favor of O_2 as an index. To determine this, let us examine the results of the tests carried out on 157 normal subjects by Benedict and his associates and shown in Table III. If "washing out" of CO_2 is a matter of practical importance, it would manifest itself by the CO_2 figures being much higher than the O_2 figures in corresponding experiments.

The average CO_2 elimination has been calculated according to decades and the average O_2 absorption similarly worked out. Next, the deviation of the CO_2 output from its average and the O_2 intake from its average were calculated for each subject.

Table VI shows the deviation of CO_2 per cent from the average in each case in which it was higher than the average. O_2 deviations are tabulated in a parallel column.

Table VI also shows that in all observations upon male subjects there is no tendency of the CO_2 output to be erratically higher than a corresponding O_2 consumption figure. Among the observations upon women one CO_2 figure is about 4 per cent higher than a corresponding O_2 figure and another one is about 2 per cent higher than a corresponding O_2 figure.

[15] *Loc. cit.*

TABLE VI

Per cent	Men		Women	
	CO_2	O_2	CO_2	O_2
Plus 22.....	....	....	1	....
Plus 20.....	....	....	....	....
Plus 18.....	....	....	1	1
Plus 16.....	....	....	....	1
Plus 14.....	1	1	....	....
Plus 12.....	111	111	11	1
Plus 10.....	1111	11	11	....
Plus 8.....	11111 1	111	1111	11111
Plus 6.....	11111	11111	1111	11111 1
Plus 4.....	11111 11111 11	11111 11111 11	1111	1111
Plus 2.....	111	11111 11111	11111	11111
Plus 0.....	11111	11111 111	11111 111	11111 1

The above table shows all positive deviations of CO_2 and of O_2 in 157 protocols (from Table III).

Out of 157 observations upon all types of normal subjects except the very young, only two showed CO_2 figures that ran distinctly ahead of corresponding O_2 figures, and in these two the deviation per cent was slight. Moreover, it is impossible to say, even in these cases, whether the O_2 or the CO_2 figure might be a better index to the heat production.

Another method of approach was used to investigate the possibility of "washing out." Observations were made upon ten unselected cases to test the effect of the preliminary period. In each case the first reading consisted of a 15-minute period, preceded by a 4-minute preliminary period; the second reading consisted of a 10-minute period without any preliminary period whatever. The results, shown in Table VII, demonstrate a negligible difference between the averages of the two sets of figures. The first two periods were used in each case, no attempt being made to select results from repeated observations.

TABLE VII

SHOWING THE CO_2 ELIMINATION FOLLOWING A PRELIMINARY PERIOD (COL. 1) AND WITHOUT PRELIMINARY PERIOD (COL. 2)

Grams CO_2 per hour (Total)	
22.36	21.48
18.88	18.78
16.92	19.74
29.32	27.66
20.56	20.82
25.92	24.48
17.68	17.28
19.44	22.20
31.16	32.52
24.76	23.52
Total 227.00	228.48
Average.. 22.70	22.85

SUMMARY

To sum up, then, what are the advantages or disadvantages of using CO_2 elimination instead of O_2 consumption as an index to basal metabolism?

1. The apparatus needed to collect and weigh CO_2 is simple and stable.

2. The method is "open." This prevents danger of possible respiratory infection, for which the "closed" methods have been criticized.

3. By weighing the CO_2 output one needs to make no corrections for temperature and barometric pressure, such as becomes necessary in using volumetric methods of O_2 consumption.

4. The psychic effect upon the patient that accrues from this open method are as follows:

A. He may be assured that he is breathing "fresh air."

B. The moving spirometer and the buzzing fan, often part of the "closed" apparatus, may form an annoyance to the patient.

5. Statistical studies upon protocols of two groups of experiments with the Atwater chamber calorimeter show a somewhat higher coefficient of correlation between CO_2 and measured calories (plus .719 and plus .846 in the two series) than exists between O_2 and measured calories (plus .488 and plus .836 in the two groups.)

6. An analysis of 157 published observations upon gas exchange showed that CO_2 is either not "washed out" during the practical application of the basal metabolism test, or else it is "washed out" in negligible amounts.

7. Results of measurements of CO_2 obtained through the method suggested in the paper corresponded closely with those published by Benedict and associates.

8. The practical application of the proposed method has been satisfactory in several hundred observations upon all types of patients. The method should not be used in diabetes because of the altered respiratory quotient in that disease.

CONCLUSION

1. A method is proposed whereby CO_2 elimination may be used as an index to basal metabolism. The apparatus is stable, simple and relatively inexpensive.

2. The CO_2 elimination seems to be at least as accurate and possibly a more accurate index to heat production than is O_2 consumption.

I feel myself much indebted to Dr. W. W. Palmer for his helpful interest in this work.

JOHNS HOPKINS HOSPITAL BULLETIN

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly. Volume XXXII is in progress. The subscription price is $4.00 per year.

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A complete index to Vols. I-XVI of the Bulletin has been issued. Price 50 cents, bound in cloth.

THE LOCALIZATION OF BACTERIA IN THE UPPER AIR PASSAGES: ITS BEARING ON INFECTION

By Arthur L. Bloomfield

(From the Biological Division of the Medical Clinic, The Johns Hopkins University and Hospital)

Despite the large amount of clinical and experimental information which we possess about the mechanism of infection, most of the details of the problem remain unsolved. We know that organisms are transmitted from one person to another by direct or by indirect means, and that in some cases disease follows the acquisition of such organisms, but the exact conditions which underlie the production of disease in the individual are still obscure. In dealing with the process of an infection entering the body through the respiratory tract we have to reckon with several distinct stages: first, the organism must be transported from some outside source to the individual to be infected; secondly, the organism after reaching the upper air passages must colonize there and not be immediately disposed of; and thirdly, it must invade the body, thus leading to the production of disease. Obviously the last two stages may, at times, be simultaneous.

It seems to us that little or no further advance in the solution of the problem of respiratory infection can be made unless we acquire accurate detailed information about the mechanism of these various stages. The laws governing the disposal of bacteria in the upper air passages, the factors which make possible colonization, and the influences which regulate the duration of carrier states must be worked out. During the past two years we have attempted to collect information of this sort by working along several lines. First, a study was made of the fate of various organisms experimentally introduced into the upper air passages.[1] The general result of this work was to the effect that foreign organisms, as a rule, are promptly eliminated, and that they can no longer be recovered in cultures made from the site of inoculation after 48 hours. It was also possible to show that the mechanism responsible for this disposal was the flushing action of the mouth secretions. The correctness of this principle has been checked in two ways: first, by clinical observation which shows that acquisition of respiratory disease often fails to occur even on prolonged and close contact exposure (for example, in lobar pneumonia); and secondly, by serial cultural studies of the throat floras of people exposed to respiratory disease which remain remarkably constant in spite of such exposure. In addition to the above-mentioned work a detailed study of the throat floras of individuals clinically normal was made.[2] Serial cultures revealed three distinct groups of organisms: first, a constant basic flora continuously present over long periods of time consisting of non-hemolytic streptococci, Gram-negative cocci, and probably diphtheroids; secondly, a transient flora of non-pathogenic or potentially pathogenic bacteria present only for short periods of time and corresponding in their behavior to that of organisms experimentally introduced; and thirdly, foreign organisms which were "carried" over long periods of time.

It seemed that the next step in the problem was to determine more accurately the mode of growth in the upper air passages of these various groups of bacteria, to discover whether they grow at large over the free surfaces of the mucous membranes or whether they are confined to special localities. This point is of especial importance in connection with carriers of pathogenic organisms. If it could be shown, as has been suggested by other observations,[3] that a chronic carrier state implies the presence of a local focus of diseased tissue in which the bacteria are breeding, the ground will be cleared for a study of the factors underlying the production of such foci.

The present study concerns itself, therefore, with the results of serial differential cultures from various parts of the upper air passages.

Material

Eight clinically healthy persons were studied. They were all workers in the bacteriological laboratory and were exposed to infectious diseases of various sorts in the wards.

Methods

Five swabs were taken simultaneously from the tongue, posterior pharyngeal wall, each tonsil, and the anterior nares. In the last case an effort was made to avoid touching the nasal orifice, and the swab was introduced about 3 cm. The swabs were spread on rabbit blood agar plates by the method already described[2] and the cultures were studied qualitatively and quantitatively.

Results

The results will be discussed from two points of view—that of various areas in the upper air passages, and that of individual organisms.

1. *The Nose.*—Staphylococcus albus was uniformly present in every culture, varying in number from a few to several hundred colonies. It seems clear that this organism may be regarded as a constant normal finding in this situation. Whether it actually lives and grows on the nasal mucosa or whether it is simply introduced from the adjacent skin surfaces one cannot say definitely. The fact that the deeper nasal passages show fewer organisms inclines us to the latter view. The white staphylococci found were both hemolytic and non-hemolytic. Diphtheroid bacilli were found in about three-fourths of the cultures. Several types were met with, and again it seems likely that they are swept in from adjacent skin surfaces. In addition to the above organisms, several other

varieties were recovered which were definitely present as transients accidentally introduced. Thus Case VIII showed five colonies of B. lactis aërogenes on one culture; Case V, six colonies of Staph. aureus on one culture; Case III, Staph. aureus on two cultures (one and two colonies, respectively); Case II, Gram-negative cocci (2 cols.) in one culture, a Gram-positive bacillus (15 cols.) in one culture; and Case VII showed Beta hemolytic streptococci on two occasions evidently introduced from the mouth, and Staph. aureus (3 cols.) at another time. Case IV carried a Staph. aureus constantly without obvious disease.

In summary, then, Staph. albus was constantly found in the nose, diphtheroids of various sorts almost constantly, and a variable transient flora of pathogenic and non-pathogenic bacteria.

2. *The Tongue.*—Gram-negative cocci of various sorts are the predominating bacteria in all the cultures. They are constantly present and clearly are members of the normal flora. Non-hemolytic streptococci are also constantly present but in somewhat smaller numbers. Diphtheroids of various sorts were encountered in about half the cultures. In no cases was any other organism repeatedly recovered from the tongue, though a few transients were picked up on single occasions—hemolytic streptococcus (once), a large Gram-positive coccus (once), Staph. albus (twice) and hemolytic influenza bacilli (eight times).

In summary, then, the flora of the tongue save for an occasional transient is simple and constant. This is to be expected, inasmuch as the anatomical structure is not such as would promote the possibility of carrier states as is so in the case of the tonsil.

3. *The Tonsils.*—Cultures from the tonsils were of special interest, since it became clear that when foreign organisms were carried their breeding place was usually here. Thus, Case V carried hemolytic streptococcus; Case I, hemolytic streptococcus; and Case II, Staph. aureus. Gram-negative cocci, non-hemolytic streptococci and diphtheroids (the normal flora) were constantly present unless obviously displaced by some foreign organism. A transient group of organisms was also encountered—Staph. albus, Staph. aureus, hemolytic streptococci, hemolytic influenza bacilli, a Gram-negative branching organism, etc.—usually in small numbers and in single cultures. It is of interest that the type of Staph. albus recovered (hemolytic or non-hemolytic) usually corresponded with that found in the nose, suggesting that the few found in the pharynx are swept back from the nose.

In summary, then, the tonsils show normal flora, transients and organisms which are carried in diseased tissue.

4. *The Pharynx.*—Conditions here correspond to those found in the case of the tonsils.

From the standpoint of individual organisms the following points may be brought out:

1. *The Gram-Negative Cocci.*—The present series of differential cultures supports the idea gained from previous work[3] that this group of organisms are normal basic inhabitants of the mouth and throat. Their wide distribution in these areas and their constant presence lead us to believe that they may lead an unaided parasitic existence on the normal mucous surfaces. This does not imply that they may never play a part in disease processes, but it seems likely that they act as secondary invaders and not as primary incitants of disease. The meningococci are for the time being excluded from these considerations.

2. *The Non-Hemolytic Streptococci.*—This group of organisms seems also definitely to fall into the normal constant flora. As seen from the tables, they are found uniformly spread through the mouth cavity, as indicated by cultures from tongue, tonsils and pharynx. We wish especially to call attention to frequent instances in which practically pure plates of these organisms are recovered from healthy individuals. It is not our purpose at present to discuss the relation of non-hemolytic streptococci to disease—the point of importance is that their mere presence in itself does not indicate an etiological relationship. A wide variety of strains is encountered judging by colony formation and morphology.

3. *Diphtheroid Organisms.*—This group was encountered in the majority of the cultures. We are inclined, despite the fact that they are not invariably present, to class them as normal inhabitants. They are for the most part slow-growing organisms, and special methods to prevent overgrowth by other bacteria show them to be almost constantly present. No attempt was made to work out the varieties of this group in detail—many kinds of diphtheroids are present in the upper air passages. Three types are especially frequent, a small, flat, dry, grey colony consisting of long forms, a glistening, grey-white bead-like colony of short stubby forms, and a very small, tough, stellate, brownish colony of minute organisms. No suggestion of pathological activity was gained from our cultures. Their significance in the upper air passages is probably similar to that elsewhere in the body.[4]

4. *Staph. albus.*—This organism, as was brought out above, is a normal habitant of the nose. It is not, however, normally present with constancy in the mouth. A few colonies were encountered from time to time clearly in the nature of transients introduced from the skin or nose. This organism may occasionally be associated with local infections (in the sinus, tonsil, etc.), in which case it is persistently present and usually in large numbers.

5. *Staph. aureus.*—This organism is not a normal inhabitant of the upper air passages. We have encountered it under two conditions: first, as a transient in nose or throat (Cases III and V); and secondly, associated with a chronic focal infection (Case II).

6. *Influenza Bacilli.*—Their significance and that of the pneumococci will be discussed in another paper.

7. *Beta Hemolytic Streptococci.*—These we have found (1) associated with acute tonsillitis or acute infections, such as influenza and scarlet fever; (2) in chronically diseased tonsils; and (3) occasionally as transients (Case VII).

The detailed results of the cultures follow:

CASE I—F

Culture	March 12	March 14	March 16	March 18
Nose	Staph. albus †(4)	Staph. albus (4)	Staph. albus (5) Beta hemol. strept. *(∞)	Staph. albus (2) Beta hemol. strept. (3) Spreader (1)
Pharynx	Beta hemol. strept. (∞) Gram-neg. cocci (6) Streptococcus-grey (6) Diphtheroid (a few)	Beta hemol. strept. (∞) Gram- neg. cocci (a few) Strept.-grey (many)	Beta hemol. strept. (∞) Strept. non-hemol. (a few) Staph. albus (1)	Beta hemol. strept. (∞) Gram-neg. cocci (a few) Diphtheroids (a few) Staph. albus (2)
Right tonsil	Beta hemol. strept. (200) Gram-neg. cocci (∞) Streptococcus-grey (many) Staph. albus (1) Staph. aureus (1) Diphtheroids (1)	Beta hemol. strept. (∞) Gram-neg. cocci (many) Strept.-grey (many)	Beta hemol. strept. (∞) Gram-neg. cocci (many) Strept. non-hemol. (many) Staph. aureus (1) Diphtheroids (many)	Beta hemol. strept. (∞) Gram-neg. cocci (many) Strept. non-hemol. (many) Staph. albus (1)
Left tonsil	Beta hemol. strept. (100) Gram-neg. cocci (sev. hundred) Streptococcus-grey (∞)	Beta hemol. strept. (∞) Gram-neg. cocci (∞) Strept.-grey (many) Strept.-green (a few) Diphtheroids (a few)	Beta hemol. strept. (∞) Gram-neg. cocci (a few) Strept.-grey (a few) Strept.-green (a few) Diphtheroids (a few)	Beta hemol. strept. (many) Gram-neg. cocci (∞) Strept.-grey (many) Strept.-green (a few)
Tongue	Gram-neg. cocci (∞) Streptococcus-grey (many) Streptococcus-green (a few) Diphtheroids (many) Hemol. influ. bac. (a few)	Gram-neg. cocci (∞) Strept.-grey (many) Strept.-green (a few) Hemol. influ. bac. (2)	Gram-neg. cocci (∞) Strept.-grey (many) Strept.-green (many)	Gram-neg. cocci (∞) Strept.-grey (many) Strept.-green (many)
Remarks	Just over a mild tonsillitis. Throat looks clear, but complains of rawness. Small clean tonsils.	Cold in nose.	Cold improving.	Well.

Culture	March 29	April 12	May 13
Nose	Staph. albus (50)	Staph. albus (12) Staph. aureus (3)	Staph. albus (8) Diphtheroids (many)
Pharynx	Beta hemol. strept. (4) Strept. non-hemol. (many) Staph. albus (6) Gram-neg. spore bear. bac. (6)	Beta hemol. strept. (∞) Gram-neg. cocci (1) Strept. non-hemol. (a few) Staph. albus (1)	Beta hemol. strept. (50) Gram-neg. cocci (a few) Strept. non-hemol. (∞) Diphtheroids (a few) Hemol. influ. bac. (many)
Right tonsil	Beta hemol. strept. (many) Gram-neg. cocci (a few) Strept. non-hemol. (many) Diphtheroids (a few)	Beta hemol. strept. (many) Gram-neg. cocci (many) Strept. non-hemol. (many)	Beta hemol. strept. (sev. hundred) Gram-neg. cocci (many) Strept. non-hemol. (many) Diphtheroids (a few)
Left tonsil	Beta hemol. strept. (sev. hundred) Gram-neg. cocci (many) Strept.-grey (many) Strept.-green (sev. hundred)	Beta hemol. strept. (very many) Gram-neg. cocci (a few) Strept.-grey (∞) Strept.-green (∞) Diphtheroids (a few)	Beta hemol. strept. (sev. hundred) Gram-neg. cocci (a few) Strept.-grey (many) Strept.-green (many) Diphtheroids (a few)
Tongue	Gram-neg. cocci (∞) Strept.-grey (a few) Strept.-green (very few)	Gram-neg. cocci (∞) Strept.-grey (many) Strept.-green (a few) Diphtheroids (a few) Hemol. influ. bac. (20)	Gram-neg. cocci (∞) Strept.-grey (a few) Strept.-green (a few) Hemol. influ. bac. (40)
Remarks	Well.	Well.	Well.

* ∞ = innumerable.

† The number of colonies is indicated in brackets.

Discussion of Case I.—This individual—a member of the hospital staff—showed no outspoken abnormalities. The nose and throat were clinically normal, save for moderately enlarged scarred tonsils. At the beginning of our period of observation he was convalescent from a mild attack of tonsillitis. A culture made one week previously had shown no hemolytic streptococci but innumerable colonies of hemolytic influenza bacilli. The cultures bring out the following points: (1) Staph. albus was constantly present in the nose; streptococcus, aureus, spreaders, and diphtheroids were met as transients. Staph. albus was at times present in small numbers in the pharynx—evidently washed back from the nose. Gram-negative cocci were almost constantly present in the pharynx, tonsils, and tongue. The same was true of the non-hemolytic streptococci. Diphtheroids were found at one or another site on each culture. Staph. aureus was twice found in small numbers in the pharynx—evidently a transient. Hemolytic influenza bacilli were found on the tongue four times, in the pharynx once. Beta hemolytic streptococci were present in large numbers in the pharynx and on both tonsils in every culture during the period of observation covering two months. It seems clear that this organism was the cause of the patient's tonsillitis and that a carrier state followed. It is of interest that the organism remained confined to a limited region and was not disseminated throughout the mouth cavity, cultures from the tongue being always negative. The presence of the hemolytic streptococcus in the nose for a few days is of interest. This was clearly an auto-inoculation, and the organism was present simply as a transient without colonization. The same has been noted in the case of other carriers.

In summary, then, the case shows the normal flora plus a Beta hemolytic streptococcus which has persisted in the tonsils following tonsillitis.

CASE II—B

Culture	March 19	March 23	March 28	April 11	May 15
Nose	Staph. albus (100)	Staph. albus (60) Diphtheroids (20) Gram-neg. cocci (2)	Staph. albus (sev. hundred) Diphtheroids (∞) Long thread-like (16) (Gram-pos. bacillus)	Staph. albus (150) Spreaders (a few)	Staph. albus. (∞) Diphtheroids (a few)
Pharynx	Gram-neg cocci (∞) Non-hemol. strept. (∞) Staph. albus (a few) Diphtheroids (a few)	Gram-neg. cocci (a few) Non-hemol. strept. (many) Staph. albus (a few) (Gram-neg.) (50) (spore-bearer)	Gram-neg. cocci (many) Non-hemol. strept. (many) Staph. albus (2) Diphtheroids (many) *Staph. aureus* (2)	Gram-neg. cocci (very many) Non-hemol. strept. (a few) Diphtheroids (a few) *Staph. aureus* (4)	Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few) *Staph. aureus* (1)
Right tonsil	*Staph. aureus* (100) Gram-neg. cocci (many) Non-hemol. strept. (many)	*Staph. aureus* (∞) Gram-neg. cocci (a few) Non-hemol. strept. (a few) Diphtheroids (a few)	*Staph. aureus* (∞) Gram-neg. cocci (few) Non-hemol. strept. (many) Diphtheroids (a few)	*Staph. aureus* (50) Gram-neg. cocci (many) Non-hemol. strept. (many) (A few cols. of a Gram-neg. branching organism)	*Staph. aureus* (∞) Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)
Left tonsil	*Staph. aureus* (200) Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few)	*Staph. aureus* (∞) Gram-neg. cocci (a few) Non-hemol. strept. (a few)	*Staph. aureus* (very many) Gram-neg. cocci (a few) Non-hemol. strept. (very many) Diphtheroids (a few)	*Staph. aureus* (∞) Gram-neg. cocci (very many) Non-hemol. strept. (many)	*Staph. aureus* (4) Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Hemol. influenza bac. (2)	Gram-neg. cocci (∞) Staph. albus (2)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Hemol. infl. bac. (50)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Gram. neg. cocci (∞) Non-hemol. strept. (a few)
Remarks	Nose and throat negative. Small clean tonsils.	Onset of severe coryza (Mar. 22). Malaise, dullness, rawness of nose and throat. Nasal occlusion with thick mucoid discharge.	Well.	Well.	Well.

Discussion of Case II.—This person was a normal control. There was no abnormality of the upper air passages save small scarred tonsils of no apparent clinical significance. Four cultures taken from this patient three months previously during the course of a cold had yielded a normal flora plus many colonies of Staph. aureus. Differential cultures were not made at the time. At the time of culture I of the present series (March 19), the patient was perfectly well. It is to be noted that the Staph. aureus was still present in the tonsils in large numbers. On March 22 a severe cold developed. It was clinically uncomplicated and the flora remained unchanged; *i. e.*, a cold occurring in a carrier of Staph. aureus. Had a single culture been made say on March 23 the state of affairs could not possibly have been interpreted. The origin of this staphylococcus carrier state is obscure. It is of interest that despite the abundance of the organisms on the tonsils there was no spread to surrounding areas. This suggests that the staphylococci were breeding in the tonsil and being discharged from within and were kept relatively localized by the overlying layer of mucus. Organisms introduced from without are promptly spread over the whole mouth cavity.

Aside from the above points nothing remarkable is noted in this case. The normal constant flora, and a few insignificant transients were recovered.

CASE III—E

Culture	March 21	March 31	April 11	April 24
Nose	Staph. albus (6) Staph. aureus (2)	Staph. albus (6) Diphtheroids (∞)	Staph. albus (20) Staph. aureus (1)	Staph. albus (many) Diphtheroids (many)
Pharynx	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Non-hemol. strept. (a few) Diphtheroids (a few) Staph. aureus (∞)	Gram-neg. cocci (a few) Non-hemol. strept. (many) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)
Right tonsil	Gram-neg. cocci (∞) Non-hemol. strept. (∞)	Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few) Staph. albus (10) Staph. aureus (2)	Gram-neg. cocci (very many) Non-hemol. strept (∞)	Gram-neg. cocci (a few) Non-hemol. strept. (many) Staph. albus (4) Staph. aureus (2)
Left tonsil	Gram-neg. cocci (a few) Non-hemol. strept. (∞) Staph. albus (2)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (many) Hemol. influenza bac. (a few) B. hemol. strept. (a few)	Gram-neg. cocci (very many) Non-hemol. strept. (many) Staph. albus (1) Diphtheroids (a few)	Gram-neg. cocci (many) Non-hemol. strept. (many)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Staph. albus (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram. neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few) Hemol. influenza bac. (3)
Remarks	Small scarred tonsils, clean superficially. Well at present.	Well.	Well.	Well.

Discussion of Case III.—This man has been under observation for over a year. During February, 1921, he had a mild attack of influenza during which a hemolytic streptococcus, which had not been present previously, appeared and persisted for about a month. At the time of the present series of cultures the patient was clinically well. The normal flora and the usual number of transients were found. On March 31 an almost pure plate of Staph. aureus was recovered from the pharynx, but this organism was found at no time thereafter. No clinical manifestations accompanied its presence. The few colonies of Beta hemolytic streptococcus present in the left tonsil on this day probably indicate a persistent infection following the attack in February. This case illustrates well the importance of serial quantitative cultures in interpreting the results of throat cultures.

CASE IV—M

Culture	March 22	April 4	April 16	May 16
Nose	Staph. albus (a few) Staph. aureus (∞) Spreaders (a few)	Staph. albus (∞) Staph. aureus (20)	Staph. albus (20) Staph. aureus (100) Diphtheroids (a few)	Staph. albus (many) Staph. aureus (many) Diphtheroids (a few)
Pharynx	Hemol. influenza bac. (40) Non-hemol. strept. (many) A large G+ coccus (a few)	Hemol. influ. bac. (a few) Non-hemol. strept. (many) Gram-neg. cocci (many) Staph. albus (1)	Hemol. influ. bac. (∞) Non-hemol. strept. (many) Gram-neg. cocci (many)	Hemol. influ. bac. (sev. hundred) Non-hemol. strept. (a few) Gram-neg. cocci (many) Staph. albus (1)
Right tonsil	Non-hemol. strept. (∞) Gram-neg. cocci (a few)	Non-hemol. strept. (∞) Gram-neg. cocci (a few) Hemol. influ. bac. (many)	Non-hemol. strept. (many) Gram-neg. cocci (many) Hemol. influ. bac. (∞)	Non-hemol. strept. (few) Gram-neg. cocci (many) Hemol. influ. bac. (∞)
Left tonsil	Non-hemol. strept. (∞) Gram-neg. cocci (a few) A large G+ coccus (a few) Staph. albus (a few) Hemol. influenza bac. (1)	Non-hemol. strept. (∞) Gram-neg. cocci (many) Hemol. influ. bac. (many)	Non-hemol. strept. (∞) Gram-neg. cocci (many) Hemol. influ. bac. (very many)	Non-hemol. strept. (many) Gram-neg. cocci (many) Hemol. influ. bac. (many)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (many) Non-hemol. strept. (a few) A large G+ coccus (∞)	Gram-neg. cocci (∞) Non-hemol. strept. (many)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)
Remarks	Well.	Well.	Well.	Well.

Discussion of Case IV.—This person—a glassware washer in the laboratory—had been under observation all winter. She had no clinical respiratory infection of any sort. No abnormality was made out in the nose or throat save small clean tonsils. The cultures showed the members of the normal flora. In addition hemolytic influenza bacilli were constantly present in the pharynx and tonsils. The patient also carried Staph. aureus constantly in the nose. This was unassociated with any obvious infection. Diphtheroids were unusually scanty. A few insignificant transients were encountered.

CASE V—H

Culture	April 8	April 12	April 19	
Nose	Staph. albus (4) Diphtheroids (20)	Staph. albus (3) Diphtheroids (Gram-neg.) (100)	Staph. albus (100) Diphtheroids (6) Staph. aureus (6)	Staph. albus (∞) Diphtheroids (a few)
Pharynx	B. hemol. strept. (∞) Gram-neg. cocci (a few)	B. hemol. strept. (20) Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	B. hemol. strept. (∞) Gram-neg. cocci (a few) Non-hemol. strept. (many) Diphtheroids (many)	B. hemol. strept. (a few) Gram-neg. cocci (many) Non-hemol. strept. (a few) Staph. albus (10)
Right tonsil	B. hemol. strept. (∞) Gram-neg. cocci (a few) Non-hemol. strept. (a few) Diphtheroids (a few)	B. hemol. strept. (∞) Gram-neg. cocci (many) Non-hemol. strept. (a few)	B. hemol. strept. (∞) Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few)	B. hemol. strept. (∞) Gram-neg. cocci (many) Non-hemol. strept. (a few) Diphtheroids (many)
Left tonsil	B. hemol. strept. (∞) Gram-neg. cocci (a few) Non-hemol. strept. (a few) Diphtheroids (a few)	B. hemol. strept. (very many) Gram-neg. cocci (very many) Non-hemol. strept. (a few) Diphtheroids (a few)	B. hemol. strept. (∞) Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	B. hemol. strept. (∞) Gram-neg. cocci (many) Non-hemol. strept. (a few) Diphtheroids (many) Staph. aureus (2)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few) Hemol. influ. bac. (100)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (many)
Remarks	Scarlet fever. Acute stage.	Throat still red.	Well.	Well.

Discussion of Case V.—This patient developed a sore throat on April 5. On April 7 a typical scarlet fever rash appeared. She did not feel very ill, and remained at work. On April 8 the rash was well out, the throat looked diffusely red, the tonsils were large, red and ragged. There was no fever at this time. The point of interest in the cultures was the constant presence of Beta hemolytic streptococci on the pharynx and both tonsils, persisting during the whole period of observation. Aside from this the normal flora and the usual number of transients were found. Hemolytic influenza bacilli were recovered from the tongue in one culture.

CASE VI—D

Culture	April 8	April 18	May 12	May 17
Nose	Staph. albus (40) Diphtheroids (many)	Staph. albus (1) Spreaders (1)	Staph. albus (75) Diphtheroids (∞)	Staph. albus (75) Diphtheroids (a few)
Pharynx	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Gram-neg. cocci (a few) Non-hemol. strept. (a few) Spreaders (1)	Gram-neg. cocci (a few) Non-hemol. strept. (a few) Diphtheroids (a few) Staph. albus (10)	Gram-neg. cocci (many) Non-hemol. strept. (many) Staph. albus (1)
Right tonsil	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few) Hemol. influenza bac. (a few) Alpha hemol. strept. (50)	Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (many)
Left tonsil	Gram-pos. coccus (∞) B. influenzæ (∞)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few) Alpha hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few)

Discussion of Case VI.—This patient has been under observation for some time. He is subject to frequent respiratory infections and has chronically diseased tonsils with large infected crypts. The cultures show nothing remarkable save a rather abundant transient flora in addition to the normal organisms.

CASE VII —B1

Culture	April 13	April 20	April 29	May 6	May 17
Nose	Staph. albus (35) Diphtheroids (many)	Staph. albus (120) Diphtheroids (6)	Staph. albus (15) Diphtheroids (a few)	Staph. albus (300) Diphtheroids (∞)	Staph. albus (200) Diphtheroids (a few)
Pharynx	Gram-neg. cocci (∞) Non-hemol. strept. (many) Staph. albus (1)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (many)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Staph. aureus (1)	Gram-neg. cocci (many) Non-hemol. strept. (v. many) Diphtheroids (very many) Staph. aureus (200)	Non-hemol. strept. (a few) Staph. aureus (∞)
Right tonsil	Spreaders (?)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Staph. albus (1) Staph. aureus (2)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Diphtheroids (many)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Hemol. influ. bac. (4) Beta hemol. strept. (10) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)
Left tonsil	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Diphtheroids (a few) Staph. albus (1)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Diphtheroids (many)	Gram-neg. cocci (∞) Non.hemol. strept. (many) Diphtheroids (a few) Staph. albus (1)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few) Staph. albus (3)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few) Beta hemol. strept. (4)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (a few) Diphtheroids (a few)

Discussion of Case VII.—This person is a laboratory worker who has been under observation over a year. He has small scarred tonsils, and has had no clinical respiratory infection during the past winter. The normal flora and the usual transients were present. In addition Beta hemolytic streptococci were recovered twice in small numbers, once from the tongue and once from the tonsil. It is of interest that this man was spending his entire time working with hemolytic streptococci. A few organisms were probably accidentally introduced into the mouth from time to time but never colonized. They fall into the group of transients. The appearance of a Staphylococcus aureus in the pharynx on three successive cultures over a period of three weeks without any clinical disease is also of interest. Had a respiratory infection developed at this time one would have been inclined to attribute it to this organism.

CASE VIII—M

Culture	April 14	April 20	April 27	May 6
Nose	Staph. albus (50) Diphtheroids (150) Lactis aërog. (5)	Staph. albus (25) Diphtheroids (a few)	Staph. albus (60)	Staph. albus (many) Diphtheroids (∞)
Pharynx	Strept. non-hemol. (∞) Hemol. influ. bac. (25)	Strept. non-hemol. (∞) Gram-neg. cocci (many)	Strept. non-hemol. (many) Gram-neg. cocci (a few) Staph. albus (1)	Strept. non-hemol. (∞) Gram-neg. cocci (∞)
Right tonsil (fossa)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (∞)	Gram-neg. cocci (∞) Non-hemol. strept. (many)	Gram-neg. cocci (∞) Non-hemol. strept. (a few)
Left tonsil (fossa)	Gram-neg. cocci (∞) Non-hemol. strept. (∞) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (many)	Gram-neg. cocci (∞) Non-hemol. strept. (many)	Gram-neg. cocci (many) Non-hemol. strept. (many) Diphtheroids (a few) Staph. albus (1)
Tongue	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (a few)	Gram-neg. cocci (∞) Non-hemol. strept (a few)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (many)	Gram-neg. cocci (∞) Non-hemol. strept. (many) Diphtheroids (many)
Remarks	Well.	Well.	Well.	Well.

Discussion of Case VIII.—This individual had had the tonsils completely removed. The normal flora and a few transients were present.

Discussion

The present work adds to the information already collected bearing on the significance of the bacteria found in the upper air passages under various conditions. Topographical cultures confirm the previous observations in regard to the normal flora and bring out the important point that the constant normal inhabitants are widely and more or less uniformly distributed through the mouth and pharynx. Other organisms occur under different conditions which have been previously outlined.[5]

The general bearings of these studies on the question of the mechanism of respiratory infection seem to us to be as follows:

(1) Aside from the normal flora, bacteria do not, as a rule, grow free on the mucous surfaces of the upper air passages.

(2) Special conditions are necessary to account for the presence of foreign organisms—either a local infection, or a transient invasion.

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THE ICE-BOX MODIFICATION OF THE WASSERMANN TEST IN THE DIAGNOSIS AND TREATMENT OF SYPHILIS[1]

By Albert Keidel and Joseph Earle Moore

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The ice-box modification of the Wassermann test consists in conducting the preliminary incubation of serum, antigen, and complement for a period of several hours at temperatures approximating 8°C., or less. This modification has been employed because of its apparent greater sensitiveness in detecting fixing substances in the sera of syphilitics. The underlying factor or factors that create this greater sensitiveness are not as yet fully understood. Several views have been advanced. It has been suggested, for example, that there are variations in the velocity and degree of complement fixation at different temperatures; that prolongation of the incubation period, such as is necessary for the ice-box test, permits more complete fixation because of the greater time allowance; that incubation of complement in the presence of antigen produces greater deterioration of the complement in the cold than incubation at a temperature of 38°C. These and other hypotheses have been investigated by various workers, but although valuable data covering these points have been obtained, a complete solution has not as yet been reached.

The literature dealing with the experimental side of the problem has recently been reviewed by Kolmer[2], who also deals with the value of the ice-box modification in the diagnosis of syphilis. As we are not prepared at this time to express opinions based on experimental evidence concerning the nature of the test, we purposely avoid a discussion of the experimental literature. This paper deals with the ice-box test from the view-point of its practical application in the diagnosis, and more especially as a guide in the treatment of syphilis.

In order properly to orient ourselves, however, we considered it necessary to determine the status of several points of contention raised by various workers in this field, and in particular, whether false positive results are obtained by ice-box incubation; and whether the results obtained with a plain alcoholic antigen in the ice-box are equal to, or better than, those obtained with a cholesterinized antigen in the water-bath.

We have therefore examined by the ice-box method 300 cases in parallel series with Wassermann tests performed according to the original technique. Our purpose is to show to what extent the two tests are in agreement with each other and with the clinical diagnoses in this series of cases; and where this agreement was not obtained, we wish to analyse the clinical evidence in so far as it supports one test or the other.

The cases are divided into three groups on the basis of clinical diagnosis and previous water-bath Wassermann tests. It is assumed that with a properly controlled technique positive water-bath Wassermanns are to be relied on for a diagnosis of syphilis. The first group contains 107 individuals composed of 30 normal persons and 77 patients with clinical non-syphilitic diseases. In the second group are 176 syphilitic patients. The diagnosis of syphilis is based on clinical, serological, and anamnestic evidence. The third group contains 17 cases, including 16 in which the diagnosis of syphilis is considered but cannot be confirmed or ruled out on the basis of clinical and other serological evidence, and one apparently normal individual with an unconfirmed history of syphilis 21 years ago.

In performing the two series of tests identical "set ups" are employed and the series are done with the same preparations on the same days, except that on account of the longer incubation in the ice-box the second incubation for completing

[1] Read before the annual meeting of the Medical and Chirurgical Faculty of Maryland, April 28, 1921.

[2] Kolmer, J. A., and Rule, A. M.: Studies in the Standardization of the Wassermann Reaction: XIV. The Influence of Temperature and Duration of Primary Incubation upon the Hemolytic Activity of Complement. Am. Jour Syph., 1920, IV, 675.

these tests is performed the next day. Both plain and cholesterinized antigens are employed in the two series, the cholesterinized antigen being prepared from the identical plain extract with the addition of 0.2 per cent cholesterin. The anti-sheep hæmolytic system is used, and the technique of performing the tests has not been varied from that in general use in our laboratory during the past 7 years. Results are recorded as positive, suggestive positive, doubtful, suggestive negative, and negative. Complete fixation only is recorded as positive. Incomplete reactions are recorded in the descriptive terms mentioned. If numerals are substituted for these terms the scale runs from zero, indicating negative, to 4, indicating positive.

Results.—The results of the investigation are as follows:

Non-syphilitic Cases.—The 30 normal individuals in this group were recruited chiefly from medical students and physicians of The Johns Hopkins Medical School and Hospital. In all of them syphilis can be excluded. Seventy-seven patients included here were affected with 44 various non-syphilitic diseases and in these also syphilis could be largely excluded, although in a few instances they had not been questioned for a history of syphilis and the examinations were not complete. In all of the 30 sera from normal individuals, the Wassermann was negative with both antigens by both methods of fixation, as it was also in 74 of the 77 non-syphilitic patients. Of the three exceptions one, a patient in whom syphilis had not been specifically searched for, gave positive tests in both series with both antigens. This patient is to be regarded as undoubtedly syphilitic on the basis of the water-bath test. Another patient, whose clinical diagnosis was achylia gastrica, gave a history of gonorrhea but not of syphilis, and the Wassermanns were negative with both antigens in the water-bath, but positive with the cholesterinized antigen only in the ice-box. The third case was one of exophthalmic goitre, in which there was no anamnestic or clinical data regarding syphilis, but the Wassermann, which was negative with both antigens in the water-bath, was positive with both in the ice-box.

TABLE I. COMPARATIVE WATER-BATH AND ICE-BOX WASSERMANNS IN NON-SYPHILITIC PATIENTS

	Total cases	Wassermann tests*				Percentage of complete agreement of tests
		0000	4444	0044	0040	
Normal individuals..	30	30	..	..	..	100.0
Various diseases.....	77	74	1	1	1	96.1
Total.....	107	104	1	1	1	98.1

*In this and the following table, results of the Wassermanns are expressed numerically, from 0 (negative) to 4 (positive), as indicated in the text. The four figures at the top of each column represent in order the results of the test with cholesterinized and plain antigen in the water-bath, and with cholesterinized and plain antigen in the ice-box. Thus, 0000 and 4444 indicate respectively all tests negative or all positive; while 0044 indicates both tests negative in the water-bath and both positive in the ice-box, etc.

Thus, of 107 presumably non-syphilitic individuals, syphilis was surely present in 1, or 0.9 per cent, and possibly present in 2 more, 1.8 per cent. The total percentage of 2.8 is sufficiently low to be well within the limits of expectation. We conclude, therefore, that in this group of patients the probability is that no false positive results were obtained, and that the ice-box method of fixation with either antigen is not too delicate.

Syphilis Doubtful.—Seventeen patients are classified in this group, four of them because of a doubtful Wassermann reaction in the water-bath, and the remainder because of the equivocal clinical diagnosis or of suggestive points in the history or examination. In two of the cases in which a doubtful water-bath Wassermann was obtained with the cholesterinized antigen only, the reaction was positive with both antigens in the ice-box. In two similar cases the ice-box reaction was anticomplementary with both antigens. In two cases the test was positive with both antigens in the ice-box though negative with both in the water-bath; while in another case a doubtful test was obtained only with the cholesterinized antigen in the ice-box. In 10 instances all Wassermanns were negative.

In all cases in which a positive or doubtful ice-box test was obtained, the clinical evidence available pointed to a diagnosis of probable syphilis, so that, in this group also, we feel that no false positive reactions occurred.

Syphilitic Cases.—This group is composed of 148 treated and 28 untreated patients. In 80 cases there was complete agreement with the two methods, with 28 positives and 52 negatives. Fifty-nine of the sera, which reacted negatively in the water-bath, were positive by ice-box incubation. In not a single instance was the ice-box test negative or doubtful when the warm incubation gave a positive. In 4 sera, however, the ice-box test was anticomplementary, two being negative and two positive in the water-bath. In the remaining 33 cases there were 2 ice-box tests with anomalous results in the plain extract reactions, and 31 instances of incomplete reactions in various combinations.

TABLE II. COMPARATIVE WATER-BATH AND ICE-BOX WASSERMANN TESTS IN SYPHILITIC PATIENTS

	Total cases	Wassermann tests									Percentage of complete agreement	Percentage ice-box pos. when water-bath neg.
		4444	0000	0044	0030 to 0042*	44aa†	00aa	4044 to 4244	1044 to 3044	Anomalies		
Treated....	148	14	50	33	20	2	2	13	13	1 (4040)	43.2	37.8
Untreated .	28	14	2	1	1	2	2	4	1	1 (4441)	57.1	10.7
Total	176	28	52	34	21	4	4	17	14	2	45.4	33.5

*Both antigens negative in water-bath; one or both in complete fixation in ice-box.
†"A"=anticomplementary.

Greater sensitiveness was exhibited by the ice-box method in 50 per cent of this entire group, but the most striking difference is seen in the greater persistence of positive reactions or some degree of fixation by this method in treated cases. In untreated cases this sensitiveness resulted in 10.7 per cent more positives, as compared with an increase of 37.8 per cent among treated cases. The plain extract in the ice-box gives

more frequent complete fixation than cholesterinized antigen in the water-bath.

The Value of the Ice-Box Test in the Treatment of Syphilis.—Since the foregoing has shown that both antigens in the ice-box secure a higher percentage of positive Wassermann reactions than either antigen in the water-bath, and that in our experience no definite false positive results were obtained, it might be expected that this modification would be of value as a control in the treatment of syphilis. So far as we have been able to determine, reference to this point is lacking in the literature.

That this is actually the case is illustrated by the curves of Chart I. For the preparation of these curves, 148 cases

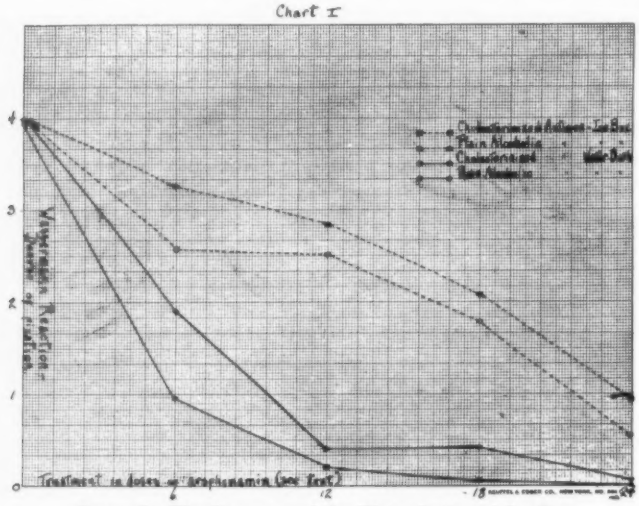

CHART I.—The Response of the Water-Bath and Ice-Box Wassermann to Treatment.

The composite Wassermanns of this chart were determined as follows: of the 148 treated patients, 61 had completed one course (6 doses) of arsphenamin. The four Wassermann tests on each of these patients were placed in vertical columns, and the numerals expressing the degree of fixation were added separately for each antigen, the sum total being then divided by the number of cases. This provides an average for the group which may be expressed as a definite fraction of the scale 0 to 4. By the same procedure, composite Wassermanns were determined at other periods during the course of treatment.

of treated syphilis, many of whom had had repeated tests by both methods, were available. Composite Wassermann reactions for each antigen were determined at arbitrary periods during the course of treatment, *i. e.*, before treatment, at the end of 6 doses of arsphenamin without mercury, and at the end of 2, 3, and 4 courses (each of 6 doses) of arsphenamin plus interim mercury. At the beginning of treatment, all Wassermanns are positive. By the end of the first course of arsphenamin, all have begun to drop toward negative, but not with the same degree of promptness. At this time, the composite test with the plain antigen in the water-bath is suggestive negative, with the cholesterinized antigen in the water-bath doubtful, while with both antigens in the ice-box it is suggestive positive. By the end of two courses of treatment, the discrepancy is even more striking. Both water-bath tests are now almost completely negative, though in the ice-box both are still of almost as great intensity as after the first course. Even after 24 doses of arsphenamin plus mercury, both ice-box tests still show some degree of fixation. The curves further provide an excellent demonstration of the relative sensitiveness of the plain and cholesterinized antigens by the two methods of preliminary fixation.

The number of cases on which these curves are based is too small to permit of final interpretation of the results. It is intended only to show that in treated syphilis the Wassermann reaction becomes negative much more slowly by the ice-box than by the water-bath method. Indeed, we have obtained in several patients, who had serologically fulfilled our requirements for the cessation of treatment with many repeated negative water-bath Wassermanns for more than a year, positive tests with both antigens in the ice-box.

These results indicate that our present standards of treatment of syphilis are probably too low, and that treatment should be continued over a much longer period of time than is now the case. The proper therapeutic control must in future include repeated Wassermann reactions by the ice-box as well as by the water-bath method. Further studies which are now being undertaken will provide more accurate data for the various types of syphilis, and will indicate, roughly at least, to what extent our present period of active treatment should be lengthened.

DISCUSSION AND SUMMARY

In presenting this study we wish to express our realization of the danger attached to modifications of the Wassermann test which tend to increase its delicacy unwisely. The mechanism by which this is accomplished at low temperature incubation is not wholly understood. If it is due to deterioration of complement in some manner dependent on factors not connected with changes in the patients' serum resulting from the disease process, its usefulness as a diagnostic procedure is vitiated. Modifications and technical fads have done much to discredit the Wassermann reaction. Incredible errors occur daily from such practices with the most distressing consequences. An erroneous diagnosis of syphilis based on a nonspecific positive Wassermann, even when subsequently corrected, leaves a trail often impossible to obliterate. A negative Wassermann resulting from technical error leaves the door open for a future diagnosis; but a false positive, particularly if followed by antisyphilitic treatment, shuts out this possibility indefinitely, if not forever.

The study which we have presented is intended to demonstrate the results of the ice-box method in cases well studied and not dependent for diagnosis on this method. Although the series is small for such a purpose, it has demonstrated to our satisfaction an important superiority in its selection of uncured treated syphilitics. Although we favor its employment for diagnosis, as yet we do so guardedly, and accept no positive results without careful scrutiny of all available data in the case.

THE INABILITY OF STAPHYLOCOCCI TO FORM INDOLE FROM PROTEIN, PEPTONE AND TRYPTOPHANE*

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Since Jordan's[1] discovery that *B. influenzæ* produces indole, attention has been directed to the other bacterial invaders of the respiratory tract which might have this function. Among these microorganisms, the staphylococci are the only ones about whose ability to produce indole there has been any disturbing uncertainty. This doubt, for example, moderated the conclusions which Jordan drew as to the utility of his discovery, and delayed the publication of the report by Rivers[2] on the value of the test for indole in the spinal fluid as an aid in the diagnosis of meningitis due to certain strains of Pfeiffer's bacillus. In order to eliminate these doubts, and in order to assist the studies on bacterial metabolism, the decomposition of protein, peptone and tryptophane by staphylococci was investigated.

On inquiry among bacteriologists, we found the opinion generally held that staphylococci produce indole. Many, however, informed us that they had never seen a positive test for indole with a culture of staphylococcus. Evidently, their opinion was based upon the unequivocal statement in the usual text-books of bacteriology, for example, Park and Williams[3] and Hiss and Zinsser,[4] where it is asserted that staphylococci produce indole in peptone water.

A careful search through the literature revealed only a scant foundation for the broad statements which appear in the text-books. The first positive evidence that certain staphylococci may produce indole was supplied by Emmerling[5] in 1896. He planted *Staphylococcus aureus* in white of egg, which he states was sterile at first and contained no contaminating bacteria during the course of the experiment. After inoculation with the staphylococcus, the egg-white was incubated under anaërobic conditions for 14 days at 37°C. Gas was formed during the growth of the culture, and at the end of the experiment indole and skatole were recognized in the distillate of the fluid. The inadequate bacteriological controls of this medium in the preparation of which there is unusual opportunity for bacterial contamination, and the unique observation of the formation of gas from the proteins of egg by *Staphylococcus*, make it seem probable that the conclusion that the indole was produced by the staphylococcus may be erroneous. In 1902, Tissier and Martelly[6] isolated from putrid meat a strain of *Staphylococcus albus* which formed indole in a medium containing fibrin. Tissier's experience seems to have been the basis for the statements of Metchnikoff, whose writings gave vogue to the opinion that staphylococci form indole. In a paper on the intestinal flora, published in 1910, Metchnikoff[7] writes: "On sait—qu'un certain nombre de microbes de la flore intestinale de l'homme produisent de l'indole. Les staphylococques et le proteus, qui tous les deux se rencontrent souvent dans la flore intestinale sont aussi de producteurs de cette substance." We have not been able to find any data in the writings of Metchnikoff to support the contention just quoted. In discussing this question, Neisser[8] remarks that this statement by Metchnikoff must be an error. Since then, the only positive report which we have found occurs in the paper by Distaso[9] in 1912, in which he described *Staphylococcus asaccharolyticus*. This was a peculiar coccus, isolated from feces. It was about twice the size of the usual staphylococcus, grew only anaërobically, had no action upon the sugars and formed indole. A review of this evidence shows that the data are insufficient to warrant the statement that indole is a usual product of the metabolism of *Staphylococcus*.

In contrast to these few questionable reports, there are a number of papers dealing with the cultural characteristics of *Staphylococcus* which present a considerable volume of negative evidence on the results of indole tests with these microorganisms. The investigators who have been unable to find indole in cultures of *Staphylococcus* are: Buard,[10] Selter,[11] Dobrowski,[12] Müller,[13] Distaso,[14] Neisser,[8] Zipfel,[15] Honing,[16] Herzfeld and Klinger,[17] Winslow, Rothberg and Parsons.[18] The number of strains of various types of staphylococci, whose failure to produce indole is recorded in these papers, is approximately 300.

SOURCES AND CHARACTERISTICS OF STRAINS STUDIED

Our report on the action of *Staphylococcus* upon media suitable for the production of indole is based upon the study of 115 strains of this organism. These strains were isolated from pathological lesions in man, human feces, air or dust and from putrid beef, as shown in the following table.

TABLE I

Source	Number of strains
Furunculosis	8
Abscesses	12
Infected wounds and ulcers	64
Osteomyelitis	2
Adenitis	3
Septicemia	3
Peritonitis	3
Conjunctivitis	3
Throat or sputum	5
Feces	7
Air or dust	4
Putrid beef	1
Total	115

All of these organisms were Gram-positive, aërobic, facultative anaërobic cocci, and grew in the usual clusters on solid

* Presented at the meeting of the Society of American Bacteriologists, at Chicago, December 28, 1920. Abstract published in *Abstracts of Bacteriology*, 1921, V. 3.

media. On Loeffler's serum, 91 strains produced a yellow or orange pigment; 24 strains were white. All reduced nitrates to nitrites. Although groupings of staphylococci on the basis of cultural reactions have not permitted a strict or helpful classification, we studied for comparison their fermentation of glucose, lactose, sucrose and mannit, and their effect upon gelatin. When these data were compiled, according to the classification suggested by Winslow, Rothberg and Parsons,[18] we found that we had representatives of all the groups noted by them and in addition three strains for which their system makes no provision. The distribution of our strains in these groups was as follows:

A. Orange pigment:
   (a) Lactose fermented, gelatin liquefied. 89 strains. (*St. aureus.*)
   (b) Lactose not fermented, gelatin not liquefied. 2 strains. (*St. aurantiacus.*)

B. White pigment:
   (a) Lactose fermented, gelatin liquefied. 14 strains (*St. epidermidis.*)
   (b) Lactose fermented, gelatin not liquefied. 6 strains. (*St. candidus.*)
   (c) Lactose not fermented, gelatin not liquefied. 1 strain. (*St. candicans.*)

The other group not included in this scheme was composed of 3 strains of white staphylococci which did not ferment lactose but liquefied gelatin.

Tests for Indole

A variety of media were used for the cultures of staphylococci on which tests were made for indole. These were 1 and 10 per cent solutions of two brands of commercial peptone, a tryptic digest of casein, egg-white, and a solution in which tryptophane was the only nitrogenous substance. Before inoculation, all of these media were free from indole, and qualitative tests with the Hopkins-Cole glyoxylic acid reagent showed that they contained tryptophane. Colon bacilli readily formed indole when growing in these solutions.

Our experience with one brand of commercial peptone indicates the necessity of rigorous preliminary tests for indole in this material before its use for cultures in which a search is to be made for this derivative of tryptophane. A 1 per cent solution of this peptone sometimes gave a faint pink or rose color with Ehrlich's reagent. When this peptone was extracted with ether in a Soxhlet apparatus, the extract had a faint odor of indole and gave a deep rose color with Ehrlich's reagent. Furthermore, the distillate of the alkaline watery solution of this peptone, according to the method of Zoller,[19] also gave a strong indole-test with Ehrlich's reagent. No attempt was made to isolate indole from this peptone, but its use was discontinued in favor of a preparation of peptone which did not give the qualitative test for indole.

All strains were seeded in these originally indole-free media and incubated aërobically at 37°C., except the series of cultures in the solution of white of egg. In this experiment, the solution of egg-white was sterilized by filtration through a No. 12 Mandler filter, tubed, incubated for 48 hours to prove its sterility, and then inoculated with all strains of the staphylococci. The tubes were placed in a vacuum jar, from which the air was removed and partially replaced by hydrogen. The anaërobic cultures were then incubated for 3 weeks at 37°C.

Tests were made with the ether extracts of fluid cultures and with the distillates of some of the cultures in peptone water. The Ehrlich reagent was used as a routine, supplemented frequently by other tests, which, however, did not equal the Ehrlich test in delicacy or reliability. This reagent was prepared as follows:

Paradimethylaminobenzaldehyde	4 grams
95 per cent alcohol	380 c. c.
HCl (conc.)	80 c. c.

In performing the test for indole, the fluid culture was shaken up with ether, and Ehrlich's reagent added so that it spread as a layer between the ether and the peptone water or other fluid. A rose color, appearing in a few seconds first in the lower part of the ether extract, indicated the presence of indole. This test has been shown to be sensitive to 1 part of indole in 1,000,000 parts of fluid.[20]

Results of Tests for Indole

Tests for indole upon the cultures of staphylococci in these media were made at intervals of 48 hours, 96 hours, 7 days and 14 days. The organisms grew abundantly in the peptone solutions and the medium made with the tryptic digest of casein. Their growth in the solution of egg-white was very scanty. The growth in the solution of tryptophane will be described in detail in a subsequent paragraph. The results of all the tests for indole upon the cultures of the 115 strains of *Staphylococcus* in these media under the conditions described above can be stated briefly: they were all negative. No evidence was obtained that any of these varied staphylococci produced even a trace of indole in media containing free or combined tryptophane.

Cultures in Solutions of Tryptophane

Zipfel [15] has pointed out that the critical test of the ability of an organism to produce indole is its cultivation in a medium containing tryptophane. The solution used by him contained asparagin and ammonium lactate in addition to tryptophane. The 8 strains of *Staphylococcus* studied by him failed to produce indole in this medium. As it is possible that the staphylococci derived their nitrogen from the asparagin and ammonium lactate, leaving the tryptophane intact, we limited the conditions more narrowly in our experiment by using a solution in which tryptophane was the only source of nitrogen. If the organism multiplied in this medium, it would be forced to obtain its nitrogen from tryptophane, the substance from which indole is formed. In the utilization of tryptophane, the organism would presumably derive nitrogen from the NH_2 group of the α-aminopropionic acid attached to the indole nucleus, as this nitrogen atom is more readily split off than the N of the pyrrole ring. In this decomposition, it is possible that the tryptophane might be deamidized only to indole propionic acid, or might be reduced further to indole. To determine which of these processes occurred in the decomposition of

tryptophane by *Staphylococcus*, the following medium was prepared:

Tryptophane (pure)	0.5 gm.
Na_2HPO_3	0.2 gm.
NaCl	0.5 gm.
$CaCl_2$	0.02 gm.
$NaHCO_3$	0.02 gm.
Distilled water	100 c. c.

This solution was sterilized by filtration through a No. 12 Mandler candle. No precipitate occurred when it was sterilized by filtration. If, however, the liquid were boiled a precipitate appeared, due probably to the formation of calcium phosphate. The reaction was Ph 7.4-7.6, without adjustment. After filtration, the flasks and tubes of media were incubated at 37° C. for 48 hours to prove their sterility. In one experiment, 0.5 per cent glucose was added to the solution. Tests for indole and indole propionic acid with this medium before inoculation were negative. *B. coli* grew readily in it, and produced indole within 8 hours.

Tubes of the tryptophane solution were inoculated with a loop of each strain of our series of staphylococci from a 24-hour agar slant culture. This made the small amount of fluid, 2 c. c., in each tube slightly turbid. In some, the turbidity increased after 24 hours and a granular sediment of organisms appeared after 4 days. At the end of 7 days, the usual tests for indole were made with each culture. These were negative.

As not all strains grew equally well in this medium, several were selected because of their more abundant growth for more detailed experiments. With them, bacterial counts were made by the dilution and plating method to show that the organisms multiplied in the tryptophane medium. Amino nitrogen and total nitrogen determinations by the Van Slyke and Kjehldahl methods were made for us by Dr. D. Wright Wilson upon the original solutions and the solutions in which the staphylococci had been cultivated. The usual qualitative tests for indole, particularly Ehrlich's test, and the ferric chloride test for indole propionic acid were applied to this medium both before its inoculation and after the growth of the staphylococci. A summary of such an experiment is shown in Table II.

This experiment demonstrated that *Staphylococcus* grew in this solution of tryptophane, that as a result of the metabolism of the coccus the tryptophane lost 17 per cent of its amino nitrogen. Indole was not formed at any period during three weeks. The solution became slightly less alkaline. The doubtful tests with ferric chloride might indicate the formation of indole propionic acid. The chemical studies show definitely that tryptophane is deamidized by *Staphylococcus*, but as yet are insufficient to prove that indole propionic acid is actually one of the substances formed in this decomposition.

TABLE II. STAPHYLOCOCCUS ALBUS NO. 115 IN 0.5 PER CENT TRYPTOPHANE

Hours after seeding	No. bacteria per 1 c.c.	Chemical analysis.
		Before inoculation.
		Ph. 7.6. Indole = 0.
		Indole propionic acid = 0.
		Total N = 0.522 gm. per 100 c. c.
		Amino N = 0.292 gm. per 100 c. c.
0	28,800,000	
1.5	29,400,000	
3	19,200,000	
4	25,600,000	
5	56,000,000	
6	144,000,000	
7	192,000,000	
8	320,000,000	
12	416,000,000	
14	410,000,000	
22.5	380,000,000	
		After 2 weeks.
		Bacteria removed by centrifuging at 2500 r. p. m. for 1 hour.
		Ph. 7.4 (approx. colorimetric).
		Indole = 0.
		White ppt. with Fe_2Cl_6 which turned red on heating. Possibly indole propionic acid?
		Total N = approximately same.
		Amino N = 0.242 gm. per 100 c. c.

SUMMARY AND CONCLUSIONS

In order to test the ability of staphylococci to produce indole, 115 strains of *Staphylococcus*, isolated from pathological lesions in man, from air, dust, human feces and putrid beef, were cultivated in media containing proteins, peptone and free tryptophane. The conditions under which the cultures were incubated at 37°C. were both aërobic and anaërobic. Numerous tests for indole with several reagents, particularly with Ehrlich's paradimethylaminobenzaldehyde solution, were made with the cultures at different intervals from 48 hours to 3 weeks. In no instance was a positive test for indole obtained. Particular significance is attached to the negative result of tests for indole with cultures of staphylococci in a fluid in which pure tryptophane was the only source of nitrogen, aside from the air, available for the growth of the organisms.

Although these results present only negative evidence, they are thought to be sufficient to warrant the conclusion that indole is not a product of the metabolism of *Staphylococcus*.

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HEMOLYTIC EXUDATES AND TRANSMISSIBLE BACTERIAL AUTOLYSIS[1]

By Jules Bordet

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What I shall say to you today cannot properly be termed a lecture; but rather a short communication bearing on some quite recently discovered experimental facts.

Among the fundamental and characteristic properties of life, the most remarkable undoubtedly are reproduction, which creates a new being, and heredity, thanks to which this new being closely resembles its parents. In fact, heredity consists in the transmission of variations, which, conferring new qualities to certain beings, gives rise to special and readily recognizable types and in this way allows of an easy discrimination between the different species, varieties, and families. What then is the intimate nature of the mechanism through which a given variation, occurring at a certain moment, may be transmitted to the offspring?

It is hardly necessary to say that every variation must perforce depend upon an immediate factor, capable of determining it directly in the cell, and which itself has been called forth by an external influence. When this external influence is permanently exerted while the cell multiplies, thus constantly causing the factor of variation to be present, it is easily conceivable that the variation itself may be conveyed from one generation to the following one, since the primary influence acts without interruption. But when the external influence is only a transient and evanescent one, disappearing at once after having brought into action the factor of variation, the transmission of the modification thus created is not so readily accounted for. Such being the case, it must necessarily be accepted that the variation could not be bequeathed through the successive generations, unless in every one of the successively engendered individuals the factor of the aforesaid variation is regularly renewed or created again and again, so as not to lose its original power and primary efficiency. In fact, were this factor not reproduced while being transmitted, of a certainty its strength would be very soon exhausted, as an unavoidable consequence of its being distributed or, if I may say so, diluted among the more and more numerous representatives of an ever-increasing offspring. Unless constantly regenerated, this factor would very soon be weakened to such an extent as to become wholly incapable of unceasingly compelling the new cells, derived from the repeated divisions, to assume the special features and aspect which for the first time appeared under its influence. It follows, then, that at the end of a limited period, the variation itself could not be transmitted any more, the factor which commands it becoming more and more attenuated as a consequence of its being progressively more and more widely distributed. As an analogy, one might say that a railway track can guide an engine to the end of its journey, precisely because it offers the same resistance and solidity all along the way, thus constantly playing an active part, that is, unceasingly repressing any tendency to deviation. Similarly, when an initial cell has been primarily modified through the agency of an external and temporary cause, the regular and henceforth everlasting transmission of the induced modification absolutely requires that the immediate factor of the latter, once created, be regularly regenerated while acting and being bequeathed.

Let us now suppose that the cell under consideration is a microörganism, and furthermore, that the direct factor of variation is an active principle which this microörganism has produced under the influence of a temporary external cause, such as a special and exceptional composition of the nutrient medium wherein it has lived during a certain period of time. Following this line of thought, we immediately anticipate that the microbe in which the variation due to this active principle has primarily occurred, will, while multiplying, bequeath to its offspring the capacity of elaborating the same substance, the indefinite persistence of the aforesaid modifications being thus insured and maintained *ipso facto* through the successive cultures. Let us imagine, moreover, that the principle alluded to is diffusible in the liquid culture medium. Such being the case, the variation now may be not only hereditary but also contagious, since the liquid in which the modified bacterium has lived contains precisely the agent capable of impressing the same modification on identical but still normal and unaltered microörganisms. These latter will be thus similarly changed, and will, moreover acquire the property of transmitting the same modification to their own offspring, or merely by means of contact to normal bacteria, and so on indefinitely. If we finally assume that the variation consists in a disturbance of nutrition, namely, in a disturbance of the equilibrium between the building of living matter and its destruction, the latter process being exaggerated, then the transmissible modification will be characterized by the fact that the organism thus changed will, henceforth, show a marked tendency to autolytic phenomena.

These views seem to be merely theoretical, but we are entitled to transfer them in their entirety into the sphere of positive and real things, of unquestionable experimental results, as I now shall try to show. As a matter of fact, they may be brought into complete harmony with experimental facts connected with the problems of immunity, which have been observed by myself and my friend and co-worker, Ciuca, and to which I shall briefly refer.

[1] Lecture III of the Herter Series, delivered before The Johns Hopkins University on Thursday, October 28, 1920.

A guinea-pig receives into the peritoneal cavity, at intervals of five or six days, two or three injections of a liquid culture belonging to the group of B. coli. Twenty-four or forty-eight hours after the last injection, the cavity is punctured and a few drops of the leucocytic peritoneal exudate are extracted. Now, this exudate possesses, as may be shown simply by adding to it a small amount of culture, the property of modifying the same colon bacillus in such a manner that it confers upon it a highly marked and henceforth transmissible autolytic power. The conflict between the leucocytic exudate and the bacterium induces the latter to elaborate a lytic substance, which, added to a normal turbid broth culture, clarifies it almost completely in the space of a few hours. Now, one droplet, or even less, of such a clarified culture, transferred into a second broth culture, normal and turbid as the first, develops in it the same process of clarification; subsequently, the second culture thus treated acts in the same way towards a third one, and so on. The experiment may be repeated again and again, one condition, however, being absolutely necessary; no transmission takes place in killed emulsions, *the culture must be living,* and if this requirement is complied with, the active principle responsible for the phenomenon is unceasingly reproduced. But, as it is found to resist a temperature of about 60-65°C., which kills the bacterium, one observes that a broth culture which has been subjected to the lytic process, and subsequently sterilized, is still able to induce the lytic influence in a living normal culture, which in turn becomes capable of transmitting it to another identical culture, and so on, as has just been told.

The technical detail is quite simple. The peritoneal exudate wherein phagocytosis has occurred, but which nevertheless still contains some living germs, is added to two or three volumes of sterile broth, the fluid thus obtained being then heated at 58°C., for nearly half an hour. Now, more broth and a droplet of living broth culture of B. coli having been introduced, the mixture is incubated. The development of the microörganism is rather difficult; only a slight turbidity appears. After having been maintained in the incubator for nearly twenty hours, the mixture is kept at the room temperature for two or three days, during which time the liquid does not become more turbid, but on the contrary shows rather a tendency to clarification. Now, when it is heated again at 58°C., it is found that a few drops of such a fluid, added to a tube of sterile ordinary broth, make the latter unfit for the growth of the colon bacillus; the nutritive medium keeps clear after being impregnated and incubated; the development is entirely hindered. On the other hand, if a few drops are introduced into a fresh and already turbid colon broth culture, clarification takes place. When the lysis has fully occurred, this culture, whether sterilized at 58°C., or not, has *ipso facto* become capable of inducing the same phenomenon in a new identical broth culture and so on, the lysogenic property being regularly and forever transmitted to the later generation of bacteria.

When a normal broth culture, already sufficiently developed, that is, showing a marked turbidity, is subjected to the clarifying influences just mentioned, it is not, in fact, completely sterilized, a certain proportion, but in reality a rather small proportion, of the bacteria which are present seem not to be affected and are still living. However, they do not grow easily in broth; when they are transplanted into a new tube of this nutrient medium, the latter becomes merely opalescent in the incubator, but—and this is a very important fact—acquires the lytic quality. Difficult in broth, the development of these germs is considerably easier and abundant on agar. After some transplantations a very rich agar culture may be obtained, the aspect of which, however, is strikingly different from that of the culture on agar of the normal unaltered B. coli. Instead of being bluish and rather thin and translucent, the agar culture of the colon bacillus which has withstood the lysis, shows an opaque, whitish and thick layer which is remarkably mucous and even semi-fluid. It is a surprising fact that this modified culture, which in reality represents a new variety, keeps permanently, even when repeatedly transplanted, the property of communicating to sterile broth, when added to it even in infinitesimal amount, the lytic character. Hence it is allowable to conclude that henceforth and forever the modified bacterium carries the autolytic property, unceasingly regenerating it while growing. It is worth mentioning that the colon bacillus transformed in that way shows also some changes in other respects. It has kept its fermentative and indole producing properties, but is no longer capable of acting on neutral broth. Its virulence, instead of having been reduced, is visibly increased. It is not so easily phagocytable as the normal original bacterium; when inoculated in sufficient amount into the peritoneal cavity of a guinea-pig it passes into the blood of the heart, always carrying its characteristic, henceforth inseparable and permanent, lytic capacity.

The phenomena just described must now be carefully confronted with the results observed by the French writer d'Herelle, which, according to this scientist, find their explanation in the presence of a living, invisible virus, the so-called "bacteriophage."[2]

In several interesting papers which have been published since 1917 in the Comptes rendus de la Société de Biologie or in the Compte rendus de l'Académie des Sciences, d'Herelle pointed out that when a mixture of broth and fæces from patients recovering from dysentery is incubated for about twenty hours and subsequently filtered, a clear fluid is obtained, possessing the wholly unexpected property of clarifying a thick suspension of dysenteric bacilli. Furthermore, a trace of such a suspension which has thus been rendered clear, added to a second suspension of the same microörganism, brings about the same effect, and so on. Similar results have been obtained by d'Herelle for other intestinal microorganisms, provided, however, that the fæces came from individuals who had recently suffered from a disease of the digestive tract or who had been associated with such patients. For example, d'Herelle obtained fluids exerting a lytic influence on

[2] We found recently that the British scientist Twort published in the *Lancet* (1915), two years before d'Herelle, a most remarkable paper in which quite analogous facts are mentioned.

a microörganism belonging to the group of the colon bacillus which was precisely the one employed in our experiments just recorded.

D'Herelle explained his findings by admitting that the lysis was due to a filterable, that is, an extremely finely divided virus, capable of living as a parasite in the inside of several bacteria such as dysentery bacilli. This virus would multiply in the bacterial bodies whenever conveyed into a new suspension. D'Herelle succeeded in demonstrating that the regeneration of the lytic agent, supposed to be a living one, did not occur in sterile broth nor in suspensions of organisms which had been previously killed. Under such circumstances, the lytic power is very soon exhausted when its transmission from tube to tube is attempted.

The experimental facts discovered by d'Herelle are unquestionable, but the explanation this writer has thought proper to offer is not correct. Objections were recently raised against it by Kabeshima, who observed that the lytic power shown by clarified bacterial suspensions obtained according to d'Herelle's indications could still be elicited and transmitted to new living suspensions even when the active fluids had been heated at about 70° C., or treated with substances unquestionably possessing antiseptic properties, such as acetone, ether or sodium fluoride.

Taking into account the well known fact that dysenteric fæces are very rich in leucocytes, and that according to d'Herelle's observations the lysogenetic property of such fæces appear only at the period of convalescence, we felt free to imagine that perhaps the lytic phenomenon observed was merely the consequence of some immunological process, or, to speak more precisely, was the result of a special modifying influence exerted by the leucocytes on the microörganisms. According to this hypothesis, the conflict between the leucocytes and the bacteria would result in inducing an hereditary vitiation of the bacterial metabolism, consisting chiefly in the production by the microörganism itself of some autolytic ferment which diffuses into the surrounding medium and consequently acts in the same way on normal bacteria belonging to the same species, when these are added to the active fluids. As I told you some minutes ago, our supposition has been fully confirmed by adequate investigation. In reality, the lytic property may, without any interference on the part of the intestinal tract or of its germs, appear in a mixture of culture and of a leucocytic inflammatory exudate containing no other living microörganism. The hypothesis advocated by d'Herelle based on the presence of a very small parasite growing inside the bacteria, if it had proved true, would indeed have been suggestive, but the correct explanation afforded by our experiments seems to be, as regards the biological significance, of still wider interest, since it offers a striking example of a nutritive modification which, once impressed through the agency of the defensive factors of the inoculated animal, is henceforth maintained and reproduced forever in the successive generations, as I emphasized above.

Whatever the method made use of to elicit the lytic property, be it the technique of d'Herelle based on the activity of the fæces of convalescents, or the experiment we performed by bringing into contact a leucocytic exudate and the bacterium, the study of the chief peculiarities of the phenomenon gives quite identical results. For example, the agar culture of the modified colon bacillus which, as I pointed out above, definitely behaves as the carrier of the lytic influence, may be obtained just as well and with the same characteristics by employing either the fluid of d'Herelle derived from the intestinal tract, or the lytic mixture which we obtained by means of a leucocytic exudate. Whatever the manner in which the active principle has appeared, its properties may be demonstrated by adding it either to an already grown broth colon bacillus culture, in which case its influence is shown by the supervening clarification, or to sterile broth containing a droplet of fresh normal colon bacillus culture, in which case the bacterial multiplication is altogether prevented, the initial fluid preserving for several days, when incubated, its original limpidity.

Another very simple and particularly striking method of detecting the lytic power consists in depositing a droplet of the lytic fluid on the surface of an incubated nutrient agar on which, living colon bacilli having been spread some hours before, a thin bacterial layer is just beginning to appear. The tube is subsequently kept in the incubator, the layer soon thickens over the whole surface, except at the points which have come in contact with the lytic droplet, growth here having been altogether inhibited and the agar surface remaining bare as before. After two or three days, however, a few colonies appear on this bare spot, consisting of resistant organisms, subsequently capable of growing abundantly when transplanted upon a fresh agar tube, assuming the special aspect described above, and preserving permanently, while unceasingly growing, the lysogenetic property.

There is no need to say that we are now going on with the experiments in order to ascertain whether analogous lytic phenomena may be, by means of our technique based on the production of leucocytic exudates, observed with several other microörganisms, belonging to saprophytic or pathogenic species. At any rate, it appears to us to be highly desirable that similar investigations be likewise carried on in other laboratories, since the question of the transmissible power of autolysis in bacteria seems worthy of the attention of the bacteriologist as well as of the biologist.

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PREGNANCY FOLLOWING IMPLANTATION OF THE OUTER END OF THE ONLY REMAINING FALLOPIAN TUBE INTO THE UTERINE CORNU AFTER RESECTION OF A CORNUAL PREGNANCY

By HENRY N. SHAW, Los Angeles, California

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(From the Gynecological Department of The Johns Hopkins University and Hospital)

I am reporting this case not because it is one of cornual or interstitial pregnancy, although these conditions are by no means common, but because as a result of a rather unusual operative procedure the possibility of conception was preserved in a case in which at a previous operation the right tube and ovary had been removed and in which at the second operation a cornual pregnancy was found on the left side. For my own part, I should not have thought of saving the outer part of the left tube, but Dr. Cullen laid it carefully aside and, after removing the cornu, inserted the proximal end of the remaining portion of the left tube into the uterine cavity. Pregnancy followed.

In the literature at my disposal I have been able to find the record of only one similar case,[1] although from time to time the inner end of the Fallopian tube has been inserted into the uterine cavity.

Gyn. No. 25283. F. L., aged 36, white, was admitted to The Johns Hopkins Hospital on October 3, 1919, complaining of irregular menstrual periods. The patient was a frail woman, weighing only 113 pounds. Her family history was good. She had had typhoid fever and malaria.

The patient had been married six years. She had had one child who had died at two years of age, and two miscarriages, one nine months after marriage at three months, and the other in March, 1919, at two and a half months.

Her last regular period had been in March. For seven weeks following this there had been no bleeding at all. After this there was a period which lasted eight days. She apparently had had a regular period four weeks before admission. A few days before the patient entered the hospital bleeding had reappeared and there has been irregular bleeding since that time. No large clots had been passed and no membranes had been noticed, but the bleeding had increased in amount.

On examination a midline scar was found below the umbilicus. There was little or no relaxation of the outlet. The cervix was lacerated. The body of the uterus was apparently normal in size and in good position. At the left cornu, however, was a rounded mass several centimeters in diameter. This appeared to be adherent to or blended with the left cornu. It was not tender and and felt rather soft. It was fairly movable. The general picture suggested a left tubal pregnancy.

Operation Oct. 6, 1919, by Dr. Cullen. The old abdominal scar was excised. On opening the peritoneal cavity an adhesion was found between the upper surface of the uterus and the lower end of the scar. This adhesion was clamped, cut and tied.[2]

In the left uterine horn we found a tumor approximately 5 x 4 cm. (Fig. 1). On the median side this blended with the surface of the uterus and on the outer side was continuous with the tube. There were enlarged blood vessels running over its surface. Undoubtedly we had to deal with a cornual or interstitial pregnancy.

Dr. Cullen temporarily clamped the tube at its cornual attachment and drew it to one side. He then resected the uterine horn leaving a raw area approximately 4 x 2 cm. at its uterine attachment. The Fallopian tube was now drawn into the uterine cornu so that its inner end lay in the cavity of the uterus (Fig. 2). The wound was then approximated. The excess of bladder peritoneum was drawn up over the raw area to prevent adhesions. After the operation was completed, the fimbriated end of the Fallopian tube, which lay free, was about 1 cm. long. One cigarette drain was placed in the lower angle of the abdominal incision and the wound closed.

The patient made a most satisfactory recovery and was discharged on October 23, 1919, just 17 days after the operation.

Gyn.-Path. No. 26637.—The growth at the left uterine cornu was 5 cm. long, 3.5 cm. broad, and projected 4 cm. from the surface (Fig. 3). It was perfectly smooth and had a delicate tracery of blood vessels covering its outer surface. Its basal attachment to the uterus was 4 x 2 cm. The walls of the sac on section varied from 1 to 3 mm. in thickness and the cavity was filled with blood (Fig. 4).

Sections through the cornual pregnancy show an outer covering of muscle varying from 1 to 3 or 4 mm. in thickness (Fig. 5). At no point does one find any evidence of an inner epithelial lining. The blood which fills the cavity extends right up to the muscle. At the junction there is some young connective-tissue formation. At some points are aggregations of polymorphonuclear leucocytes and small round cells. Here and there are perfectly free spherical cells that have taken up brown pigment. In the center of the blood-clot is an early placenta with an amniotic sac in its center. The chorionic villi are typical.

On Dec. 28, 1920, I received a letter from the patient saying:

I am getting along very nicely. I was threatened with an abortion at two months, but have been very careful since then, and have had no further trouble.

[1] Plastic Operation on the Fallopian Tubes, by Emil Ries, American Jour. Surgery and Gynecology, March, 1899, Vol. XI, p. 180.

Ries says: "Occlusion at the uterine end of the tube is produced quite frequently by small adenomyomas of the tube, but there is only one case on record where an operation was performed for such an occlusion. This operation was performed by Dr. T. J. Watkins of Chicago, and I gave the first short notice of it in my paper on Nodular Forms of Tubal Disease (Jour. Experimental Medicine, 1897). This operation practically amounts to an end to end anastomosis between the tube and the uterus—a salpingo-hystero-anastomosis. It was performed so that the myomatous nodule was excised by a wedge-shaped incision reaching down into the cavity of the uterus, the tube then being implanted into this opening and retained by sutures. The appendages on the other side had been removed on account of pyosalpinx. The patient miscarried a number of months after the operation, proving thereby that the salpingo-hystero-anastomosis had kept patent the communication between the tube and uterus."

[2] In 1918, at another hospital, the uterus had been suspended, and the right tube and ovary removed. The adhesion extending from the upper surface of the uterus was undoubtedly due to the old suspension.

On March 21, 1921, I received a letter from her saying:

Soon after writing you last I began having bearing down feelings. Dr. Porter had me go to bed and gave me something in case the pains began. I was in bed two weeks and finally lost my baby on the 11th of March. The baby was seven months or a little over. A fine child and well developed. Dr. Porter did everything he could to ward off labor but nothing did any good. The afterbirth came first and it was a foot presentation.

Dr. D. S. Porter of Andrews, S. C., this patient's family physician, under date of April 25, 1921, kindly sent me further particulars. He said:

I had to keep her in bed the greater part of the time and was under the impression that the pregnancy was further advanced than she claimed, as the uterus at the time of her confinement was on a level with the costal margin.

There was a marginal placenta prævia and a breech presentation. The baby was premature, I should judge about seven months. It was born dead.

In the Gynecological Department Dr. Cullen has for years been urging the utmost conservatism where pelvic inflammatory conditions exist during the child-bearing period, and wherever possible has preserved the menstrual function, feeling that in many cases the unsexing of the woman in early or early middle life was more deleterious to her than the thought or probability of an occasional second abdominal operation.

In this case the logical procedure seemed to be removal of the left tube with the cornual pregnancy, but the saving of the outer portion of the tube and its insertion into the uterine cavity proved well worth while.

The patient was most anxious to become pregnant again and had it not been for the placenta prævia she would in all probability have gone to term. We shall look forward with interest to the subsequent history of this patient as she is still under forty.

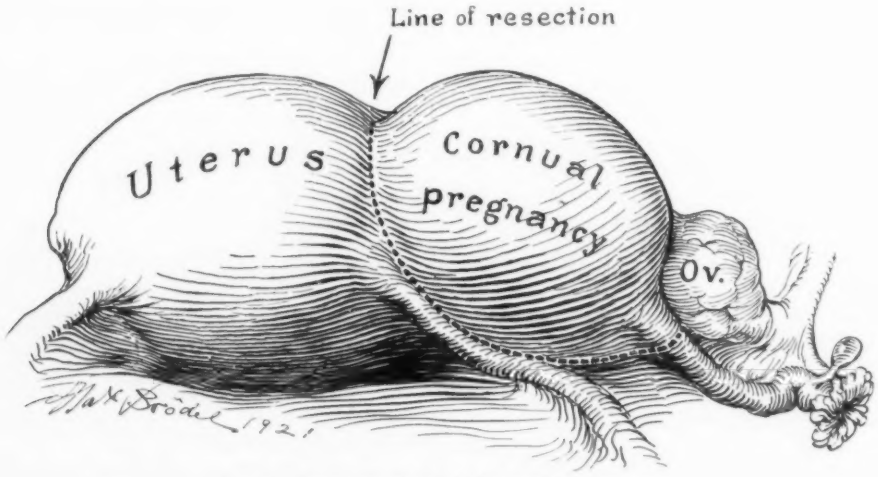

FIG. 1.—Resection of a Left Cornual Pregnancy.

Gyn. No. 25283. The right appendages had been removed at a previous operation. The left cornual pregnancy was cut away, as indicated by the dotted line. For the subsequent handling of the left tube see Fig. 2. For the appearance of the cornual pregnancy see Figs. 3, 4 and 5.

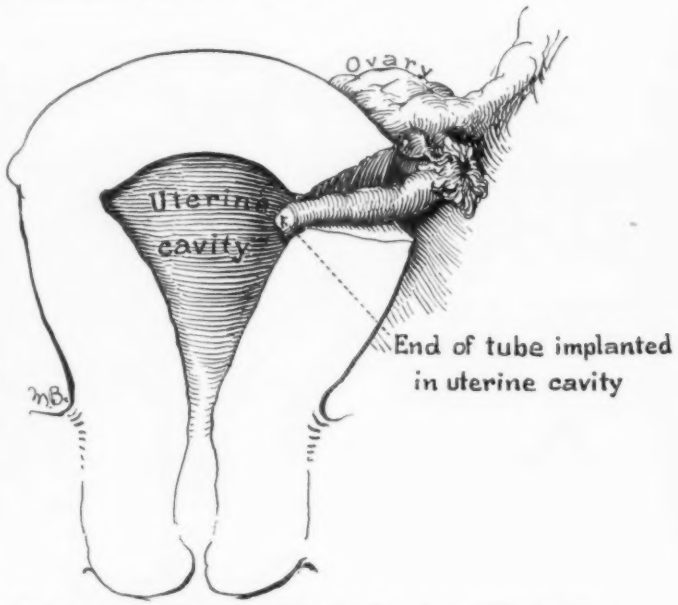

FIG. 2.—Implantation of the Fallopian Tube into the Uterine Horn.

Gyn. No. 25283. The right tube and apparently the right ovary had been removed elsewhere at a previous operation.

The outer end of the left tube seen in Fig. 1 was drawn into the uterine horn until its inner end lay in the uterine cavity. The cut edges of the uterine horn were now snugly approximated with catgut. About 1 cm. of the outer end of the tube then lay free in the abdomen. Pregnancy soon followed through this tube.

FIG. 3.—Pregnancy in the Left Uterine Horn.

Gyn. No. 25283. Gyn.-Path. No. 26637. The left and under surface represents the uterine attachment of the cornual pregnancy. A small piece of the left tube has been removed with the cornu. For the appearance on section see Fig. 4.

FIG. 4.—A Left Cornual Pregnancy.

Gyn. No. 25283. Gyn.-Path. No. 26637. This is a longitudinal section through Fig. 3. There is a thin outer wall of muscle. The greater part of the specimen consists of old blood. Fig. 5 shows that the central portion of the clot contains placental tissue.

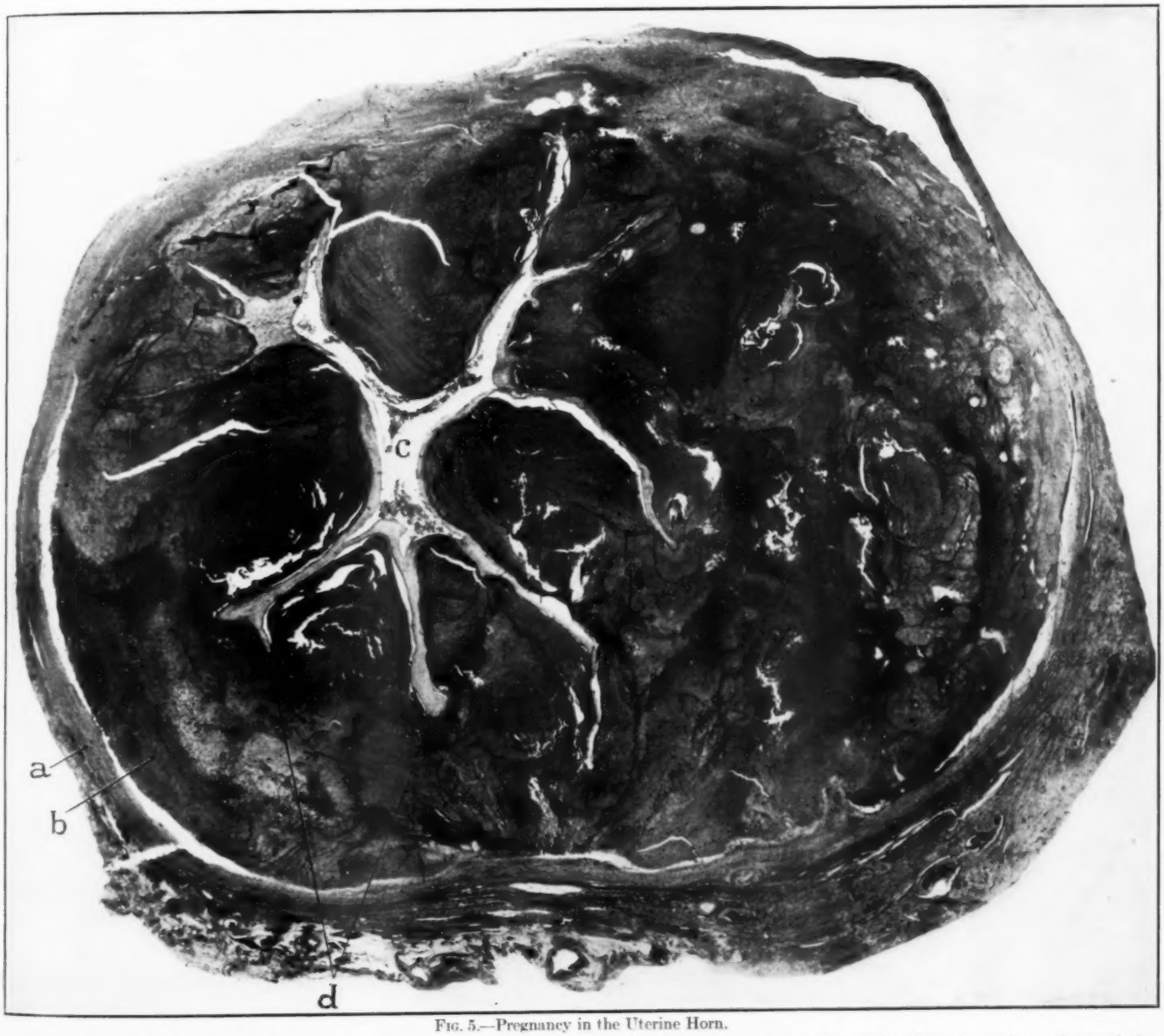

FIG. 5.—Pregnancy in the Uterine Horn.

Gyn. No. 25283, Gyn.-Path. No. 26637. This is Fig. 4 enlarged five times. *a* is the outer muscular wall; *b* the blood-clot filling the cavity; *c* the amniotic sac containing some granular material. Extending out into the blood-clot are numerous placental villi, two of which are indicated by *d*.

NOTES ON NEW BOOKS

The Diseases of the Genital Organs of Domestic Animals. By W. L. WILLIAMS. Pp. 856. (Ithaca, N. Y., 1921.)

This large volume by the professor of obstetrics and of research in the diseases of breeding cattle in the Veterinary College of Cornell University is highly creditable to its author and represents a valuable contribution to American medical literature. I earnestly recommend it to scientifically minded obstetricians and gynecologists, as I feel sure that when they have read it they must agree with me that they have learned much, have had their imagination stimulated, and have to confess, so far at least as certain problems are concerned, that human gynecologists may learn something from their veterinary colleagues.

Space will not permit a complete review of this excellent work, and consequently I shall dwell upon only a few points which have particularly interested me. After a satisfactory account of the normal anatomy of the male and female generative organs of cattle, including a fairly accurate section upon the structure of the placenta, the author takes up the changes which occur in disease, and shows that in both sexes, but particularly in the female, many lesions occur with which we are familiar in human beings.

In considering the estrual cycle, the author is a firm believer in the regulatory function of the corpus luteum, and points out that estrus will not set in so long as the corpus luteum of the last period persists. Accordingly, whenever it is delayed, he advocates squeezing the old corpus luteum out of the ovary by pressure exerted through the rectum, which within three days is followed by the appearance of estrous symptoms. Indeed, he goes a step further, and states that whenever the induction of abortion is indicated in cows, it can be most readily effected by the same maneuver, which he holds is practically infallible and far more efficacious than the procedures formerly employed. Such observations go far toward establishing the Fraenkel-Born theory concerning the function of the corpus luteum, and appear difficult to reconcile with the fact that in women the removal of an ovary containing the corpus luteum does not bring about the termination of pregnancy after the first few months.

The removal of the corpus luteum by rectal manipulation naturally suggests the methods of gynecological diagnosis in the cow, of which rectal palpation is the most important. By its means it is possible to recognize not merely the existence of pregnancy as early as the end of the second month, or even to diagnosticate the presence of twins, but also to palpate the tubes and ovaries and to detect the presence of tumors, persistent corpora lutea or other abnormalities. Vaginal exploration is employed to a lesser extent, but what is said concerning the inspection of the cervix, as well as concerning intrauterine manipulations, is very suggestive of human gynecology.

To those unacquainted with veterinary medicine possibly the most interesting portion of the book is that dealing with venereal disease in domestic animals. Thus, the author describes the vesicular and the granular venereal diseases of cattle, which likewise occur in goats and swine; dourine and horse pox in horses; venereal granulomata and catarrhal venereal disease in dogs; and, finally, an inflammatory venereal disease which affects rabbits. All of these diseases are definitely due to coital infection.

Although only a few words can be said concerning certain of them, it will surprise most laymen to learn that 90 per cent of the cattle in this country are suffering from granular venereal disease, from which they rarely recover completely, as well as the fact that most other domestic animals are liable to venereal disease of some sort. Such knowledge will be regarded as a stumbling block by many "uplifters," and particularly by those who regard the existence of venereal disease as a specially devised punishment for sexual sin, and who regard any steps which may be advocated to bring about its abolition as tending to popularize sexual immorality. If they feel thus toward man, what must they say concerning the mild-eyed cow, which is almost universally infected, or concerning the harmless rabbit which frequently becomes infected at the time of mating?

It was a surprise to me to learn that dourine has been observed in horses in this country, and it will surprise many to be told that this very fatal disease is due to infection by a trypanosome, which, instead of being transmitted by the bite of an insect, is conveyed from animal to animal by sexual intercourse, and, furthermore, that its presence can be detected in the blood and spinal fluid of the infected animal. Likewise, it is interesting to learn that the venereal granulomata of dogs are thought to be due to a spirochete, which, however, bears no relation to that causing syphilis.

Certainly the most important section of the work, in the estimation of the author, is the one dealing with infections of the generative tract. The average medical man is vaguely aware that cows and other domestic animals occasionally suffer from puerperal infection, analogous to that observed in women, and that epidemic abortion may cause great economic losses to stock raisers, and is currently believed to be due to infection by a specific micro-organism, the bacillus abortus of Bang. Williams, however, believes that while this bacillus may sometimes lead to abortion, it is not the only organism concerned. On the other hand, he holds that its significance has been greatly over-estimated, and that the general acceptance of its specific character has served to obscure the issue, as well as to prevent the recognition of the fact that the problem is much more complicated than is generally believed. He states that abortion may be caused by any one of a number of micro-organisms, including the bacillus abortus, and that most cattle suffer from such infections before they become pregnant, so that the occurrence of abortion, dystocia, retention of the fœtal membranes or actual puerperal infection depends upon the virulence of the infection, as well as upon the resistance offered it by the infected animal. In this connection Williams holds that identical bacteria are concerned in the production of various inflammatory diseases of the male genitalia, so that coitus between healthy and infected animals is extremely dangerous for the normal partner, whether male or female, and that infection thus established constitutes a serious danger not only for the individual concerned, but for the entire herd.

Furthermore, the consequences of such infections are not limited to the genitalia of the animals involved, but in many instances the bacteria gain access to the fœtus in utero and cause its death, or lead to the birth of congenitally infected offspring. The mode of fœtal infection is of great interest. Except in the presence of the most virulent infection, the author believes that the placentomata of the cotyledonary placenta offer an efficient barrier against the transmission of bacteria from the mother to the fœtus. On the other hand, he assumes that the portions of the chorion between the cotyledons are very vulnerable to bacterial invasion and readily permit the passage of bacteria into the amniotic cavity, where they may be swallowed by the fœtus and lead to its infection. Evidence to this effect is afforded by the fact that the same bacteria can be found in the stomach and intestinal tract of the dead fœtus as in the maternal uterus, and that pellets of meconium containing similar bacteria are present in the liquor amnii. As the latter are normally absent, he attributes their presence to diarrhœa from which the fœtus had suffered while still *in utero*. Furthermore, in the case of animals which are born alive, the existence or the prompt development after birth of dysentery, pneumonia or pyæmia clearly points to intrauterine infection.

While Williams apparently makes out a clear case for the occurrence of congenital infections in cows and sheep, it is questionable whether they occur in human beings. Owing to the different structure of the bovine and human placenta, the relations existing between the uterine wall and the fœtal membranes differ greatly, so that what may hold good in the cow will not necessarily apply to human beings. It must, however, be remembered that the observations of Slemons upon the

development of placental bacteriæmia, in certain cases of intrapartum infection in women, make it possible that we may have overlooked a possible source of antenatal infection, and, consequently, Williams' observations should stimulate us to renewed investigations along such lines.

In cases of relative sterility and abortion the microscopical study of the anatomical structure and peculiarities of the spermatozoa of the bull are likewise very suggestive. Williams points out that in certain instances actively motile spermatozoa may present abnormalities, which, while not sufficient to interfere with impregnation, may so influence the vitality of the ovum after fertilization as to lead to its early death and subsequent expulsion. In human beings we tend to focus our attention too exclusively upon the maternal aspects of the problem, and it is quite possible in certain cases of repeated abortions occurring in women with normal genital organs that careful study of the spermatozoa might show that the essential factor is paternal.

The few points mentioned will suffice to indicate that this work is not a treatise for relatively ignorant cow or horse doctors, but rather that it is based upon careful observation and study, and can more than hold its own in competition with many text-books upon human gynecology and obstetrics. Whether all of the conclusions of the author are correct or not I am not in a position to judge, and in many respects it is a matter of indifference, but I can say that the book has interested me immensely, and has demonstrated that the problems of veterinary medicine are as interesting as those of human medicine, and that both can be solved only by the same methods of painstaking and careful scientific work.

J. Whitridge Williams.

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